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CONTENTS AND SUBJECT INDEX

Meningococcic Meningitis and Acute Meningococcemia. C. V. Craster, M.D., and Henry Simon, M.D., Newark, N. J. 1069
Vascular Accidents of Extremities. Géza de Takáts, M.D., Chicago. 1075
Effect of Vitamin B_1 on Peripheral Neuritis of Pellagra. Tom D. Spies, M.D., and Charles D. Aring, M.D., Cincinnati 1081
Treatment of Metastatic Carcinoma of the Neck Secondary to Carcinoma of the Lip. R. B. Moreland, M.D., Hines, Ill. 1084
Pulmonary Complications After Cyclopropane. G. Edgar Burford, M.D., New York 1087
Massive Atelectasis Following Cyclopropane Anesthesia. Oswald R. Jones, M.D., and George Edgar Burford, M.D., New York 1092
The Identification of Gonococci in Complications of Gonorrhea. R. J. Reitzel, M.D., and Cordula Kohl, B.S., San Francisco 1095

CLINICAL NOTES

Serum Carditis. Eugene Clark, M.D., New York 1098
A Case of Intestinal Heterophyidiasis of Man in Hawaii. Joseph E. Alicata, Ph.D., and O. L. Schattenburg, M.D., Honolulu, T. H. ... 1100
Duodenal Ulcer as a Cause of Death in a Case of Meningococcic Meningitis. Carl A. Hartung, M.D., Chattanooga, Tenn., and Josef Warkany, M.D., Cincinnati ... 1101
Recurrent or Residual Progressive Ileitis. Gordon D. Oppenheimer, M.D., New York 1103

SPECIAL ARTICLE

Chemical Aspects of Riboflavin. Lela E. Booher, Ph.D., Washington, D. C. 1105

COUNCIL ON PHYSICAL THERAPY 1111

COUNCIL ON PHARMACY AND CHEMISTRY 1111

EDITORIALS

Wheeler-Lea Bill Giving Federal Trade Commission Jurisdiction over Foods, Drugs, Devices and Cosmetics Becomes a Law ... 1112
A New Source of Blood for Transfusion 1113
Synergic Effects of Antigens ... 1114

CURRENT COMMENT

Commercial Aspects of J. Thompson Stevens—a "Miracle Man" ... 1114
Thiamin Chloride and Nicotinic Acid in Pellagra 1115
Governor of Kentucky Praises American Physicians 1115

BUREAU OF LEGAL MEDICINE AND LEGISLATION 1139

(Subject Index on next page)

ORGANIZATION SECTION
Facing page 1154
Meeting of Committee on Supply of Medical Service 169B
Progress of Study of Medical Care 170B
The British Health Services .. 170B
Medical Legislation 174B
Official Notes 175B
Woman's Auxiliary 175B
Medical Economic Abstracts .. 176B

A. M. A. SESSION - San Francisco - JUNE 13-17, 1938

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Full Details in SAUNDERS ADVERTISEMENT—Page 3

SUBJECT INDEX TO THIS ISSUE

The letters used to explain in which department the matter indexed appears are as follows: The Star (*) indicates an Original Article; "ab," abstract; "E," Editorial; "C," Correspondence; "Ml," Medicolegal; "ME," Medical Economics.

A. M. A. Annual Congress on Medical Education and Licensure....1131
Abell, Irvin, to receive Laetare Medal....1117
Abortion, criminal, janitor performs....1117
Acid, nicotinic, in pellagra....E-1115
salicylic acid, skin absorption of....C-1127
Addison's Disease, cevitamic acid for....1121
Adrenals, hemorrhages, Waterhouse-Friderichsen syndrome....*1071
Allegheny County Medical Society, pediatric survey....1119
American Academy of Arts and Sciences to award Amory Septennial Prize....1119
Medical Golfing Association tournament..1119
Aminopyrine, agranulocytosis from....1129
Amory Septennial Prize....1119
Androgens, testosterone proprionate in hypogonadism; resent publicity....C-1128
Anemia, essential hypochromic, in gynecology....ab-1151
Anesthesia, cyclopropane, massive atelectasis after....*1092
cyclopropane, pulmonary complications..*1087
ether, compared with cyclopropane....*1088
Aneurysm, intracranial, compression of chiasma, optic nerves and tracts....ab-1149
Antigens, synergic effect of....E-1114
Armstrong, Robert B., honored....1117
Arteries hemorrhage, traumatic, in extremities....*1075
Arthritis, chronic, bee venom treatment..ab-1143
identifying gonococci in....*1096
mono-articular, as initial manifestation of meningococcic meningitis....*1073
Atrophy, muscular, heredity....1122
Bacteremia, identifying gonococci in....*1096
Beach, Rex, article on Dr. J. Thompson Stevens....E-1114
Bedbugs, lichen urticatus from....ab-1152
Benzedrine sulfate as cycloplegic....1131
Beriberi, work of Sir Thomas Stanton....1120
Blackboards, yellow....1120
Blood coagulation factors in hemorrhagic disease....ab-1145
collection and preservation for mailing....1130
phosphatase, elevation in disease....ab-1146
pressure, action of insulin vs. metrazol.ab-1153
transfusion, donors investigated, Germany.1122
transfusion, placental blood for.E-1113; ab-1148
uric acid in gout....ab-1143
vessels, accidents in extremities....*1075
vessels disease, mecholyl iontophoresis in.1129
Board Examinations....1134
Book Notices....1135
Books Received....Adv. page 32
Brain, tuberculous foci in....ab-1142
Breast cancer and purulent discharge from nipple....1129
Bureau of Legal Medicine and Legislation..1139
Burky Phenomenon....E-1114
Car sickness, psychiatric study....ab-1142
Chandler A. B., praises American physicians....E-1115
Cleveland Medical Library Association....1118
Correspondence....1127
Cosmetics, Wheeler-Lea Bill....E-1112
Council on Medical Education and Hospitals....1131
Council on Pharmacy and Chemistry....1111
Council on Physical Therapy....1111
Deaths....1124
De Lamar Lectures....1117
Detwiler, Samuel R., gave Ferris Lecture..1116
Diabetes Mellitus, insulin in....1129
insulin resistant....ab-1153
Diagnosis centers for low income classes....1121
Digestive Tract diseases, course on....1116
Diphtheria carriers....1131
heart in....ab-1149
Drugs, absorption through skin....C-1127
Wheeler-Lea Bill....E-1112
Embolism, arterial traumatic....*1076
Endocarditis, identifying gonococci in....*1096
Enzyme, yellow, relation to riboflavin....*1105
Epinephrine, sensitization to....1130
Erythema nodosum as allergic reaction..ab-1154
Estrogens during menstrual cycle....ab-1142
Eugenics and medicine....1120
Extremities, vascular accidents....*1075
Eyes, swelling around, after sea bathing....1130
Ferris Lecture in anatomy....1116
Fever, low-grade: nasopharynx infection.ab-1145
Fish, raw, intestinal heterophyidiasis from.*1100
Food poisoning, alpha type streptococci in.ab-1145
Wheeler-Lea Bill....E-1112
Foreign Letters....1124
Gonorrhea, complications, identification of gonococci in....*1095
treatment, sulfanilamide....ab-1151
Gout, uric acid in....ab-1143
Health unit, first full time, Colorado....1116
Heart disease, improved diagnosis....1122
disease, roentgen therapy of thyroid...ab-1150
disease, velocity of circulation relation to basal metabolism....ab-1150
in diphtheria....ab-1149
serum carditis....*1098
Hemorrhage, blood coagulation factors in.ab-1145
Herpes stomatitis....ab-1145
Heterophyidiasis, intestinal....*1100
Homatropine as cycloplegic....1131
Hospitals, in general: nurses; liability for negligence of....Ml-1140
Chicago Hospital Association and Chicago Hospital Council merge....1117
Indian hospital dedicated....1119
records; impeachment of medical witness....Ml-140
Hyperthyroidism, roentgen therapy....ab-1152
Indiana University School of Medicine....1117
Infants, illegitimate, care of, Netherlands..1123
Insulin, crystalline, action on blood pressure and electrocardiogram....ab-1153
Intestines, heterophyidiasis from eating raw fish....*1100
recurrent or residual progressive ileitis..*1103
Iron, parenteral administration....1131
Jelliffe, Smith Ely, honored....1118
Joslin, E. P., to address Chicago Medical Society....1116
Kiehl, Heman B., honored....1117
Kugler, Joseph C., honored....1117
Laetare Medal, Dr. Abell to receive....1117
Lead poisoning in cigar makers....1123
Leprosy research, Queen Wilhelmina Institute; first congress....1123
Lescohier, A. W., new president of Parke, Davis and Company....1119
Leukocytes, count, central nervous regulation....ab-1153
Leukoplakia and cancer of cervix....ab-1141
Licensure, professional....ab-1131
Lichen urticatus from bedbugs, etc....ab-1152
Lips cancer, metastases to neck....*1084
Liver diseases, hippuric acid test in....ab-1150
peritonitis, cause of death in....ab-1147
Lungs, complications after cyclopropane...*1087
echinococcic cyst....ab-1151
massive atelectasis after cyclopropane...*1092
Lymphogranuloma Venereum, diluted Frei antigen for....ab-1147
virus....ab-1149
Marriage, Australian premarriage clinic....1120
Marriages....1123
Masturbation in 2 year old boy....1130
Measles, detecting Koplik's sign in, with ultraviolet ray....1131
inclusion bodies....ab-1144
unusually prevalent, Chicago....1117
Mecholyl iontophoresis, apparatus for....1130
iontophoresis in vascular disease....1129
Medical Association of State of Alabama...1116
Medical Examinations and Licensure....1134
Medicolegal Abstracts....1139
Meetings, Coming Meetings....1140
Meningitis, meningococcic....*1069
meningococcic, duodenal ulcer as cause of death....*1101
meningococcic, vaccination against....ab-1141
tuberculous....ab-1142
Meningococcemia, acute....*1069
Menstruation cycle, estrogens during....ab-1142
Methyl Salicylate, absorption through skin.C-1127
Metrazol vs. insulin, action on blood pressure and electrocardiogram....ab-1153
Mononucleosis, infectious, Wassermann test in....ab-1141
Narcotics: cannabis; possession of growing plant illegal....Ml-1140
Nasopharynx infection, low-grade fever..ab-1145
Neck cancer, treatment....*1084
Nerve, optic, compression of chiasma, nerves and tracts....ab-1149
Nervous system disorders and mumps...ab-1154
Neuritis, peripheral, of pellagra, effect of vita. in B_1....*1081
New and Nonofficial Remedies....1111
New York University, gift to....1118
News....1116
Nipple, purulent discharge from, and cancer.1129
Norris, Edgar H., professor of pathology..1117
Northern Tri-State Medical Association....1118
Ointment, absorption through skin....C-1127
Pancreatitis, acute, pancreatropic hormone in....ab-1151
Parke, Davis and Company, Dr. Lescohier new president....1119
Parotitis and later nervous disorders....ab-1154
Patella, slipping, tendon transplant for...ab-1148
Pearl, Raymond, to speak on longevity....1116
Pediatrics, Allegheny County Medical Society survey....1119
Pellagra, peripheral neuritis of, effect of vitamin B_1....*1081
thiamin chloride and nicotinic acid in...E-1115
Peptic Ulcer, duodenal ulcer as cause of death in meningococcic meningitis....*1101
painful crisis, histamine for....ab-1150
Peritonitis, liver, cause of death in....ab-1147
Petrolatum, absorption through skin....C-1127
Physical Examinations: plaintiff in personal injury suit; rights of defendant....Ml-1139
Pituitary, pancreatropic hormone in pancreatitis....ab-1151
Placenta, blood for transfusion..E-1113; ab-1148
Pneumoconiosis, cruising X-ray laboratory for silicosis tests....1118
Poliomyelitis, serum carditis....*1098
Psychiatry, scholarship in....1119
Purpura haemorrhagica fulminans....ab-1147
haemorrhagica, splenic irradiation in...ab-1143
Queries and Minor Notes....1128
Reading test using yellow blackboards....1120
Respiratory Tract infections and streptococcus vaccines....ab-1141
Riboflavin, chemical aspects....*1105
Roentgen Rays, rotation irradiation....ab-1152
Ryle, J. A., delivered Galton lecture on medicine and eugenics....1120
St. Joseph Clinical Society....1118
Saliva, Zambrini's reaction....ab-1150
Scarlet Fever, intracutaneous toxin immunization....ab-1144
Schools, medical, in the university....ab-1132
Sea bathing, swelling around eyes after...1130
Selenium poisoning....C-1128
Shock, mechanism....ab-1143
Skin, drug absorption through....C-1127
Sleep, viosterol for narcolepsy....ab-1154
Society Proceedings....1140
Specialties, functions of special boards...ab-1133
Spleen, irradiation in hemorrhagic purpura....ab-1143
Stanton, Sir Thomas, death....1120
Staphylococcus septicemia, antitoxin for..ab-1146
State Board Examinations....1134
Stevens, J. Thompson....E-1114
Stomatitis, herpetic....ab-1145
Streptococcus, alpha type, in food poisoning....ab-1145
hemolytic, from normal throats....ab-1145
vaccines and respiratory infections....ab-1141
Sulfanilamide, action in gonorrhea....ab-1151
Surgery, Zambrini's ptyaloreaction in...ab-1150
Syphilis, healthy child of parent with....1128
serodiagnosis, Laughlen test....1128
Temperature, high human: 110 F....C-1127
Thiamin chloride in pellagra....E-1115
Throat, septic sore, outbreak, New York..1118
Thrombosis traumatic, in extremities....*1078; *1079
Tobacco, plumbism in cigar makers....1123
Tonics and Sedatives....Adv. page 26
Tonsils, tuberculosis....ab-1154
Trombidiosis....ab-1152
Tuberculin sensitization by intracutaneous injection....ab-1145
Tuberculosis, campaign against, France....1121
erythema nodosum as allergic reaction..ab-1154
mortality in Netherland East Indies....1123
sanatorium, Governor Chandler's dedicatory remarks....E-1115
Undulant Fever, transfer from one human to another....1131
University, medical school in....ab-1132
Uterus, cancer (cervical) and leukoplakia.ab-1141
Veins hemorrhage, traumatic, in extremities.*1079
Viosterol therapy of narcolepsy....ab-1154
Vitamin B_1, effect on peripheral neuritis of pellagra....*1081
B_1 in pellagra....E-1115
Warren, Shields, lectures in Atlanta....1116
Wassermann Reaction in infectious mononucleosis....ab-1141
Wheeler-Lea Bill....E-1112
Woman's Medical College of Pennsylvania, 88th anniversary....1118
Workmen's Compensation Acts: Bell's palsy....Ml-1139
Wounds, cutaneous healing in....ab-1148

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MENINGOCOCCIC MENINGITIS AND ACUTE MENINGOCOCCEMIA

A CLINICAL STUDY

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AND
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Night City Physician
NEWARK, N. J.

The syndrome produced by the meningococcus organism when it attacks the meninges remains unconquered. One is impressed by its low incidence and high mortality as contrasted with those of other contagious diseases, such as measles and varicella, which have a high incidence and a low mortality. Persons who have not had measles or chickenpox will contract the disease because they have not acquired immunity by having had it. In the case of meningococcic meningitis, only infrequently does one of the many persons exposed to the disease contract it, although about one half of the persons exposed during epidemics become carriers of the organism.

One cannot sit complacently and boast about the tremendous advances in curative and preventive medicine, because the mortality of meningococcic meningitis in the first year of life is still about 50 per cent. In the accompanying table the mortality in Newark, N. J., for the past nineteen years is shown to range from 75 per cent in 1923 to 25 per cent in 1926, 40 per cent in 1932 and 46.8 per cent in 1936. It averaged 44.4 per cent. This figure represents 572 cases, with 254 deaths, including those at all ages. In 1918 there were 102 cases, in 1930 fifty-three, in 1935 eight and in 1936 forty-seven.

Epidemics of meningococcic meningitis tend to appear every ten years in certain localities. This is not true of Newark. A wave of epidemic proportions might strike Newark. It is for this reason that an effort must be made to perfect those measures which will tend to lower the death rate. Our paper has been written with this purpose in mind, namely, to attempt to contribute and to emphasize certain fundamental phenomena, which, when observed at the bedside of the patient, will mean an early diagnosis of meningococcic infection and the early use of effective therapeutic procedures.

Dr. Ellis L. Smith of the Isolation Hospital of Essex County permitted the utilization of case histories, and Dr. Harrison S. Martland, chief medical examiner of Essex County, the quotation of autopsy reports. Dr. Josephine B. Neal, chief of the meningitis division of the department of health of New York City, offered valuable suggestions. Dr. Horace Bell, resident at the Essex County Isolation Hospital, verified the diagnosis in cases in which the patient was sent to that hospital. The late Dr. Frank W. Pinneo of the Babies Hospital cooperated in the report of case 3.

There are two theories as to how the meningococcus reaches the meninges. One is that the meninges are invaded by direct extension through the cribriform plate of the ethmoid bone, with the original source of the organism in the nasopharynx. The other is that the organism passes from the nasopharynx into the blood stream and thence to the meninges. Many authorities favor the latter theory. They say that blood cultures are positive before the meninges are invaded and before the spinal fluid becomes cloudy. They add that there are many cases of infection of the blood stream (meningococcemia) without the production of meningitis.

We are going to present some clinical data stressing the rash in meningococcic meningitis. There is a specific rash, just as there is a rash for measles or scarlet fever. However, this rash occurs in only 10 to 15 per cent of the cases. The spots are petechial or purpuric. They occur before the beginning of the meningeal signs, that is, before the spinal fluid becomes cloudy, and disappear by the third or fourth day unless unusually extensive. By the third or fourth day the spinal fluid has in most cases become cloudy. This phenomenon is caused by bacterial emboli in the stage of bacteremia. A massive purpuric rash occurs when the condition is fulminating. The petechiae may be found on any part of the body, most frequently on the extremities. They look like flea bites; hence the term "spotted fever" has been given to this disease. They do not fade on pressure, vary from pinpoint to one-half inch in diameter, often being irregular in shape, and, when they fade, leave a rusty stain.

McLean [1] stated that in 83 per cent of his cases he was able to obtain smears showing intracellular meningococci by puncturing a petechial or purpuric lesion with a needle and staining the resultant drop of blood, smeared on a glass slide, with the Gram stain.

Josephine B. Neal [2] stated that this may be a difficult bacteriologic test and that it may be necessary to wait for the results of the culture of the blood. At times gram-positive organisms are pleomorphic and will decolorize with the Gram stain. Sometimes the meningococcus on an initial smear will not decolorize and appear gram positive. The importance of a smear from a petechial or purpuric lesion is demonstrated by the fact that if gram-negative organisms are obtained a quick diagnosis of meningococcemia may be made, before the blood culture has grown and before any change has taken place in the spinal fluid. A purpuric or petechial rash should, even in the absence of any meningeal sign, enable one to foretell that meningitis

1. McLean, Stafford, and Caffey, John: Endemic Purpuric Meningococcus Bacteremia in Early Life: Diagnostic Smears from the Purpuric Lesions, Am. J. Dis. Child. **42**: 1053-1074 (Nov.) 1931.
2. Neal, Josephine B.: Meningococcic Meningitis in Children, J. A. M. A. **105**: 568-571 (Aug. 24) 1935.

may develop in the near future. Numerous diseases have an accompanying purpuric or petechial rash. A rash due to the presence of the meningococcus requires the finding of that organism. Petechial and purpuric rashes occur when the blood platelets are deficient (thrombocytopenic purpura). Secondary purpura may be due to poisons, such as mercury, arsphenamine and benzene. Infections such as subacute bacterial endocarditis and hemorrhagic forms of the exanthems produce cutaneous

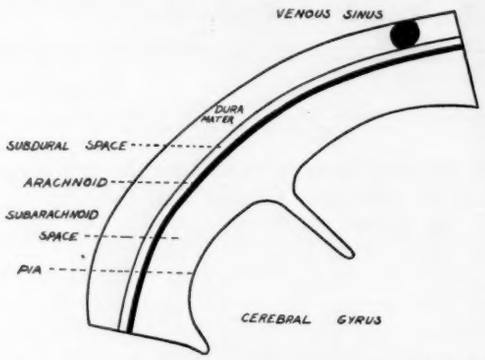

Fig. 1.—The meninges (reproduced from figure 257 in Howell, W. H.: A Textbook of Physiology, ed. 9, Philadelphia, W. B. Saunders Company, 1927).

hemorrhages. Severe anemia, leukemia or hemophilia may cause purpura. It is therefore obvious that a meningococcemic purpura requires the identification of the etiologic gram-negative diplococcus.

Like the exanthems, certain atypical rashes may occur with cerebrospinal fever. Herrick [3] mentioned a maculopapular rash resembling the roseola of enteric fever. Holt [4] stated that a general erythema or a morbilliform eruption closely resembling measles may be present. Osler described an erythema, dusky mottling and rose-colored hyperemic spots like the typhoid rash.

Boone and Hall [5] reported a case of fulminating meningococcic septicemia in which a direct blood smear, taken for a routine white cell and differential count, when stained with Wright's stain revealed numerous intracellular and a few extracellular diplococci; the blood culture was positive for meningococci. Thus it is evident that a nonpurpuric skin may harbor meningococci in the cutaneous capillaries, which are demonstrable by obtaining a drop of blood by needle puncture of the skin. This blood is spread on a glass slide and stained with Wright's stain, methylene blue or Gram's stain.

Herrick [3] and Burton and Chalmers [6] emphasized the fact that the presence of a purpuric rash means fulminating meningococcemia. In the case reported by Burton and Chalmers, extensive purpura, associated with hematemesis and melena, was followed by the death of the patient nineteen hours after the onset of illness. A petechial rash means a less fulminating infection than does purpura.

The blood count shows from 15,000 to 60,000 leukocytes, with 90 per cent polymorphonuclears.

Miller [7] reported a case in a 2 week old child who had giant vesicles filled with cloudy fluid on the abdomen, upper part of the right thigh and groin. Meningitis developed. Dr. Horace Bell has observed herpetic vesicles on an erythematous base in meningococcic infection. The characteristic location is the lips and the face, but the eruption may be anywhere. It is the most frequent eruption and is common in older children but rare in infants. Tillett and Brown [8] cited a case in which a confluent herpetic rash on the lips and inside the mouth preceded by several days the appearance of meningeal signs. A smear of fluid from a herpetic lesion may show meningococci. Herpes may appear at any time. The herpes accompanying meningitis must not be confused with herpes zoster. Herpes is rarely seen before the fifth day.

Positive blood cultures have been obtained in from 25 to 30 per cent of cases. If patients are seen early, in the stage of bacteremia, before the spinal fluid becomes cloudy or when the spinal fluid has been cloudy for a short time, a much higher percentage of positive blood cultures will be obtained. This explains the figures given by Herrick,[3] who stated that as many as 80 per cent of blood cultures may be positive. This fact is made use of in the therapy at the Essex County Isolation Hospital, where serum is given intraspinally only, and not intravenously, when the spinal fluid is cloudy, because at this stage blood cultures are usually negative.

Certain characteristics of the spinal fluid should be studied when a meningococcic infection is present. The spinal fluid is usually hazy or cloudy. There is an increase in globulin. The sugar is diminished or absent. There is leukocytosis with polynucleosis. The meningococci may be demonstrated with a Gram stain as being either intracellular or extracellular. Very early and very rarely does the physician encounter a case in which he gets a clear spinal fluid. The explanation is obvious. The meningococci have not yet migrated from the blood stream to the spinal fluid. In a case of this kind, if one will wait from twelve to twenty-four hours and repeat the tap, a hazy spinal fluid will be obtained.

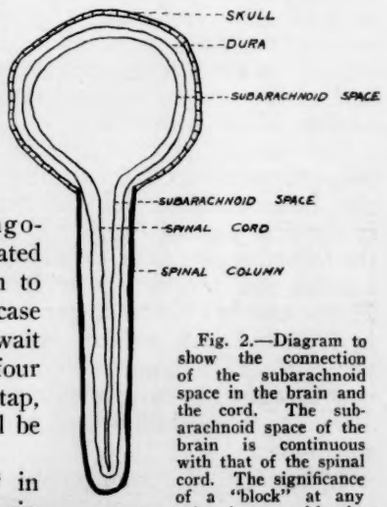

Fig. 2.—Diagram to show the connection of the subarachnoid space in the brain and the cord. The subarachnoid space of the brain is continuous with that of the spinal cord. The significance of a "block" at any given level is shown, with the necessity of tapping at a higher level than the block in order to drain the spinal fluid. (Reproduced from figure 258 in Howell: A Textbook of Physiology.)

Tillett and Brown,[8] in an analysis of twenty-six cases, mentioned a case in which meningococci were cultured from a spinal fluid which in other respects was normal. It was clear, with 2 cells per cubic millimeter. Serum was given intravenously and the patient recovered.

The meningococcus is the only organism that disappears quickly from the spinal fluid. Often it is difficult to find both by smear and by culture, so that a clinical rule has been evolved whereby one is justified in giving antimeningococcus serum in any case in

3. Herrick, W. W.: Cerebrospinal Fever, in Cecil, R. L., and Kennedy, Foster: A Textbook of Medicine, Philadelphia, W. B. Saunders Company, 1927.

4. Holt, Emmett, and McIntosh, Rustin: Holt's Diseases of Infancy and Childhood, ed. 10, New York & London, D. Appleton & Co., 1933.

5. Boone, J. T., and Hall, W. W.: Meningococcus Septicemia with Report of Case Showing Organisms in the Direct Blood Smear, U. S. Nav. M. Bull. **33**: 446-451 (Oct.) 1935.

6. Burton, A. G., and Chalmers, D. K.: Purpura as a Sole Sign in a Case of Meningococcus Septicemia, Lancet **1**: 296-297 (Feb. 8) 1930.

7. Miller, D. J. M.: A Case of Meningococcus Meningitis in the New-Born with Interesting and Unusual Features, Arch. Pediat. **34**: 824 (Nov.) 1917.

8. Tillett, W. S., and Brown, T. M.: Epidemic Meningitis: Analysis of Twenty-Six Cases, Twenty-One of Which Occurred in the Spring of 1935, Bull. Johns Hopkins Hosp. **57**: 297-316 (Nov.) 1935.

which the spinal fluid is hazy or cloudy when the etiologic organism cannot be found. The diminution or absence of spinal fluid sugar is characteristic of a meningococcic infection. When the sugar content tends to return to normal the patient is on the road to recovery. One of the earliest signs that a recrudescence or relapse is about to manifest itself is the lowering of the sugar content of the spinal fluid when the patient is apparently well on the road to recovery. Herrick [3]

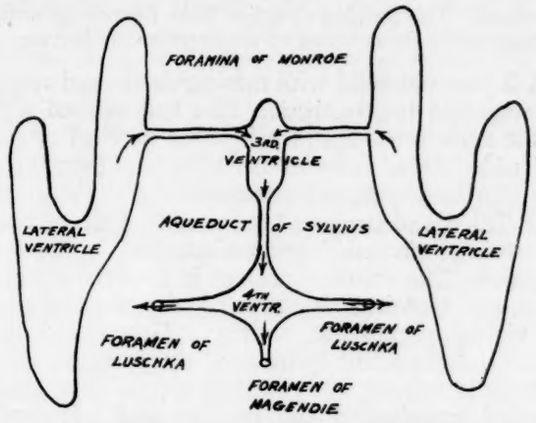

Fig. 3.—Circulation of the cerebrospinal fluid. The arrows show the direction of the flow. (Reproduced from figure 260A in Howell: A Textbook of Physiology.)

stated that recrudescences and relapses occur in from 20 per cent to 30 per cent of the cases, so it is apparent that the quantitative estimation of spinal fluid sugar as a matter of routine is of definite clinical importance in the prognosis. In conjunction with this lowering of the sugar content of the spinal fluid in a recrudescence and relapse there are a return of the organisms to the spinal fluid and a reappearance of the hazy or cloudy appearance of the fluid.

It is often difficult to obtain fluid by spinal puncture from the new-born or young infant owing to the formation of a block in the narrow foramina or subarachnoid space by inflammatory exudate. The spinal fluid may coagulate in the needle. Cisternal punctures or ventricular punctures should be resorted to.

We are presenting case reports showing (1) the Waterhouse-Friderichsen syndrome, (2) the mental changes in patients with meningococcic meningitis, (3) mono-articular arthritis as the initial phase of cerebrospinal fever and (4) the difficulties encountered by the clinician in the diagnosis of meningococcic meningitis in infancy.

WATERHOUSE-FRIDERICHSEN SYNDROME

The Waterhouse-Friderichsen syndrome is really acute fulminating meningococcemia associated with adrenal hemorrhages. It cannot be distinguished clinically from fulminating meningococcemia; the finding of adrenal hemorrhages on postmortem examination serves as the differential diagnosis between the two conditions.

Four cases occurred in the Aldridge family:

CASE 1.—Vivien A., aged 5 years, admitted April 7, 1936, for possible scarlet fever with pharyngitis, had as chief complaints sore throat, abdominal pain, aching joints and fever. She did not appear acutely ill. The temperature was 104 F., the pulse rate 134 and the respiratory rate 30. The temperature dropped to 101.8 F. the next day but subsequently rose to 104 and reached its peak of 104.8 three days after admission. Thereupon it dropped, and it stayed normal until the patient was discharged April 29. The blood culture was reported positive for meningococci on April 10. The final diagnosis was meningococcic septicemia and acute pharyngitis.

CASE 2.—Lawrence A., aged 2½ years, admitted on the same day as his sister, Vivien, appeared normal. The temperature, pulse and respirations were normal. There were no physical abnormalities. For three days the child's condition remained unchanged. On April 11 the temperature shot to 104.8 F. The patient looked toxic but the lungs were clear and there were no neurologic signs. Petechiae were seen over the elbow and the abdomen. A blood culture was positive for meningococci. Fourteen cubic centimeters of antimeningococcus serum was administered intravenously, but the child went into shock in spite of a negative sensitivity test. The next day petechiae appeared over the entire body and in the bulbar portion of the conjunctiva of the right eye. No Brudzinski sign or contralateral reflex was elicited, but there were questionable stiff neck and a questionable bilateral Kernig sign. Spinal tap showed a cloudy fluid (12,700 cells, with 97 per cent polymorphonuclears). Serum was given intraspinally. After a stormy course the child recovered, and he was discharged on May 9, after being at the hospital one month.

CASE 3.—Bernard A., aged 1½ years, was admitted April 9, 1936, moribund, stuporous and cyanotic, with a temperature of 105 F. The parents did not notice that the child was sick until 3 a. m. the night before admission, when he appeared to have a fever.

Neurologic examination gave negative results except that it showed slight rigidity of the neck, a slight Kernig sign and no rash. The hemoglobin content was 59 per cent, and a blood count revealed 4,200,000 red cells and 14,250 white cells, with 54 per cent lymphocytes.

The patient died on the day of admission. Autopsy showed the classic appearances of the Waterhouse-Friderichsen syndrome.

The brain was characterized by acute encephalitis with pia-arachnoid edema. It was moderately wet, the gray matter throughout the cortex and the basal nuclei was pinkish and there was no meningeal exudate over the top of the brain. The pons, medulla, fourth ventricle and cerebellum were soft and pink, with no gross exudate. Meningococci were cultured from material obtained from the pia-arachnoid by inserting a swab made from a sterile platinum loop. Both adrenal glands showed medullary and cortical hemorrhages. Other pathologic changes were cloudy swelling of the liver, kidneys and heart and hyperplasia of the thymus.

McLean and Caffey [1] and other investigators have demonstrated that children having an enlarged thymus and a "status thymicolymphaticus constitution" are least resistant to the meningococcus organism.

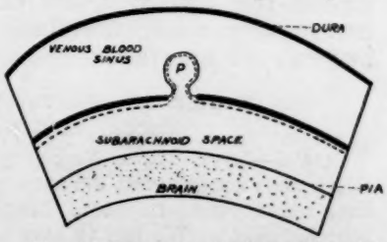

Fig. 4.—Pacchionian bodies (arachnoidal granulations). Since the subarachnoid space is a closed cavity filled with the cerebrospinal fluid which is secreted by the choroidal glands, some means of egress must be furnished for the fluid. This exit is provided by a system of filters called the pacchionian bodies (*P*). (Reproduced from figure 260 in Howell: A Textbook of Physiology.)

CASE 4. — Richard A., aged 3½ years, had a short history of illness and died at home. The postmortem appearances were the same as those of his brother Bernard (case 3).

Dr. Martland accepted in these cases a diagnosis of fulminating meningococcic meningitis with bilateral adrenal hemorrhages. It must be remembered that there is no gross exudate in the meninges. The infection is so fulminating that often the child dies in the septicemic stage with a clear spinal fluid and no meningeal signs.

CASE 5.—A woman, aged 42, was admitted in a coma and died shortly afterward.

Autopsy showed petechiae in the brain but no gross exudate of meningitis. Petechiae were present in the kidneys, intestine and heart; there was no endocarditis. Petechiae and hemorrhages were seen in both adrenal glands. The lungs showed no pneumonia. Meningococci were obtained from the pia-arachnoid by inserting a sterile platinum loop, thus establishing the diagnosis of the Waterhouse syndrome, which requires the finding of meningococci, hemorrhages in the adrenals and a fulminating infection, with death often occurring before a purulent meningeal exudate develops.

In some cases of this syndrome the resistance of the patient is strong enough to ward off death, permitting the invasion of the meninges, with the formation of a definite purulent meningeal exudate and cloudy fluid. An autopsy must be performed in these cases to establish the presence of adrenal hemorrhages. McLean and Caffey [1] said that the cause of early death is adrenal hemorrhage, which produces a clinical picture of marked prostration with intense cyanosis and shock.

In one of Aegerter's [9] patients, a 7 year old boy, the following pathologic changes were observed post mortem: Petechiae were present in the mucosa of the mouth, larynx, stomach, intestine and skin and hemorrhages from 1 to 3 mm. in diameter throughout the peritoneum, pleura and pericardium; the adrenals were almost as large as the kidneys and were purple; the capsules were tense with blood; the brain was wet and heavy but showed no overt meningitis. Death had occurred ninteen hours after the initial symptom.

Only fifty-six cases had been reported in the literature up to May 1936. Examination of the spinal fluid gave relatively negative results; in only six cases did it demonstrate the presence of meningitis. The absence of a cloudiness of the spinal fluid was due to the fulminating nature of the disease and the quick death of the patient, who died before purulent meningitis occurred.

Treatment of the Waterhouse syndrome depends on early diagnosis with immediate intravenous use of meningococcus serum. The presence of adrenal hemorrhages and depletion of the sodium ion in the blood, with symptoms of adrenal failure (hypotension, weakness, low blood sugar content and circulatory collapse), suggest that adrenal cortex extract, dextrose given intravenously, epinephrine, fluids (saline solution given by vein) and transfusions be used.

THE CHANGE IN MENTALITY IN MENINGOCOCCIC MENINGITIS

CASE 6.—David W., a Negro, aged 40, was drowsy, fell asleep when not disturbed, did not answer any questions put to him, resisted any attempt to examine him and refused to open his mouth. We had to have a man hold his head and another hold his hands so that we could pry his jaws apart to look into his mouth. He preferred to lie on his side with his legs drawn up. No matter how we shouted at him he refused to answer or cooperate. He was too weak to sit by himself. He had a boardlike rigidity of the neck. Bilateral Kernig and Brudzinski signs were elicited. His knee jerks were hyperactive. He resisted having his temperature taken. His pulse rate was 120 and his blood pressure 130 systolic and 70 diastolic. He resisted our looking at his pupils, refusing to open his eyelids. His abdomen was soft. Spinal tap showed cloudy fluid with a cell count of 7,200, polymorphonuclears 60 per cent, globulin 4 plus and the sugar content diminished. Examination of a smear gave negative results, but culture showed meningococci.

This case illustrated well the loss of mentality; the septic adult brain became the brain of a 2 year old child who would not answer questions and resisted examination. Herrick [3] stated:

> The patient is dull, apathetic, indifferent; he plaintively resents disturbance, responds in monosyllables with the expenditure of a minimum amount of energy, and prefers to lie on the side with knees drawn up and head bent forward. There is no modulation of voice or play of expression. Silence and immobility are striven for and active delirium or coma are infrequent. This striking deviation from the normal mentality at once arrests the attention of the experienced observer.

A 2 year old child with meningitis showed the mental state and hyperesthesia. She had marked rigidity of the neck, screamed in pain when handled or moved and when the stiffness of her neck was demonstrated. She remained quiet and asleep if not disturbed.

In Tillett and Brown's [8] series, almost all the twenty-six patients presented acute alterations in the mental faculties. The delirium present in fourteen either was short and transient or consisted of prolonged periods of violent purposeless activity. Generalized hyperesthesia was present in most of the patients. Hyperesthesia is present when there is a painful response to physical examination and nursing care. It produces excessive crying, resistance to examination and exaggerated reflexes and may be so intense that any movement of the body causes agonizing cries. The patient is greatly disturbed and cries lustily on hearing a loud noise or being exposed to a bright light. Ravid [10] described the crying as being incessant and brought about by the slightest touch, as though pain was evoked. The peculiar, intense, high pitched cry has been termed "the hydrencephalic cry of increased intracranial pressure."

Occasionally, as illustrated by Holt and McIntosh,[4] there is at the beginning of meningococcic meningitis no loss of mentality whatever, the patient being mentally alert, as was demonstrated by the following case, which we observed at the Newark Salvation Army quarters:

CASE 7.—Joseph D., aged 48, admitted with pain in the back of the neck and frontal headache of two days' duration, had done no vomiting but was anorexic. The physical examination showed that he was mentally alert. He had a temperature of 102 F., his neck was very stiff, and bilateral Kernig and Brudzinski signs were elicited. The spinal fluid was cloudy, with 8,000 cells per cubic millimeter. This man was not disturbed mentally by the presence of meningitis. He was not drowsy, as was David W., who showed extreme drowsiness, but he also died.

CASE 8.—Daniel R., a Negro, aged 31, a chicken plucker by occupation, had a history of chills and fever initiating the onset of illness. He was irrational and uncooperative and kept talking about plucking chickens. He reassembled and pecked at the bedclothes as though he were removing feathers from chickens, maintaining an intermittent delirious chatter. The neck was very stiff. The pupils were dilated and did not react to light. The patient resisted examination, and the mouth could not be opened. A spinal tap showed the presence of meningococcic meningitis; the patient died.

CASE 9.—Raymond B., a Negro, aged 17, was delirious; he screamed loudly, was extremely excitable and kept repeating the words "mama-pap" "one-two." He was irrational, showed marked carphologia and resisted examination. There was a boardlike rigidity of the neck, and spinal tap showed the cloudy fluid of meningococcic meningitis. The patient recovered.

9. Aegerter, E. E.: Waterhouse Friderichsen Syndrome: Review of the Literature and Report of Two Cases, J. A. M. A. **106**: 1715-1719 (May 16) 1936.

10. Ravid, J. M.: Meningococcic and Nonmeningococcic Meningitis in New-Born and in Young Infants, Am. J. Dis. Child. **49**: 1282-1298 (May) 1935.

In conclusion, we may state that the foregoing case reports illustrate extreme drowsiness, delirium producing an irrelevant chatter, resistance to examination, inability to answer questions and hyperesthesia.

MONO-ARTICULAR ARTHRITIS AS THE INITIAL MANIFESTATION OF MENINGOCOCCIC MENINGITIS

CASE 10.—Jeanette P., aged 6 years, was admitted with a history of two days of pain in the right elbow. The tentative diagnosis was rheumatic arthritis of the right elbow or "observation meningitis." On the second day the temperature was 105 F. The patient was drowsy, complaining of headache, and had slight resistance of the neck but no real rigidity. Petechiae appeared. On the third day there were definite stiff neck and Kernig and Brudzinski signs. Spinal tap showed the cloudy fluid of meningococcic meningitis.

This case clearly shows some of the difficulties the clinician may experience in making an early diagnosis of meningitis. During the first two days of illness the child had a mono-articular involvement of the right elbow, with a fever and no neurologic signs pointing definitely to meningitis. When the petechiae appeared, on the second day, meningococcic bacteremia was suspected.

Carnot [11] mentioned a triad of manifestations of meningococcemia consisting of "intermittent fever, arthralgia, and a hemorrhagic eruption."

CASE 11.—Robert H., a Negro, aged 5 years, was admitted with pain and tenderness in the right knee. The knee was so tender that it could not be touched, but it did not appear swollen; he cried when it was moved. A tentative diagnosis of rheumatic arthritis of the right knee was made. The temperature was 101 F. on the first day of illness. The next day severe headache and nonprojectile vomiting developed, but the right knee was not as tender as before. On the third day the child kept his head turned to the right and had classic meningeal signs. The temperature was 103 F. A spinal tap showed cloudy fluid with a cell count of 5,680 and 90 per cent polymorphonuclears, globulin 3 plus and sugar absent. A smear of spinal fluid showed meningococci. The patient recovered.

This boy had no meningeal signs the first two days of his illness, which means that one must be suspicious of meningitis when an illness is initiated by tenderness and pain in one joint followed by headache and vomiting.

Tillett and Brown described the syndrome of polyarthritis that occurred in nine of their twenty-six patients. The joints showed pain, swelling and signs of fluid. In six cases a joint was tapped and the fluid was thick, cloudy and rich in polymorphonuclears; in three cases meningococci were cultured from the fluid. Herrick [8] mentioned that acute arthralgia or polyarthritis is often an initial symptom and that an erroneous diagnosis of purpura rheumatica (Schönlein's purpura) may be made, owing to the combination of joint pain, tenderness and purpuric spots with no obvious meningeal signs. Indefinite pain in the joints, particularly in the knees, may mean meningococcemia, with meningitis developing from two to four weeks later. The knees are involved most frequently and the wrists next. Applebaum stated that chronic meningococcic septicemia may start with arthritic symptoms. In some cases the arthritis is present at the onset of the disease, while more frequently it appears as the meningitis is beginning to subside. There may be pain in the joints without any external evidence of inflammation. Joints, the seat of meningococcic arthritis, usually completely recover, with no permanent disability.

11. Carnot, Paul: Rev. gén. de clin. et de thérap. **46**: 97 (Feb. 13) 1932.

MENINGITIS IN INFANCY

The following cases illustrate diagnostic criteria for meningitis in infancy:

CASE 12.—A boy, aged 3 months, had a peculiar cry, nystagmus and bulging fontanel. The neck was not rigid and the Kernig sign was not elicited. There was a Brudzinski sign. The temperature was 104 F. Spinal tap yielded cloudy fluid from which meningococci were isolated.

The absence of rigidity of the neck and of Kernig's sign are characteristic of meningococcic meningitis at this age.

CASE 13.—John Mc., aged 4 months, admitted with a temperature of 104 F. and a purpuric and petechial rash over the legs, abdomen and chest, was drowsy and his eyes showed nystagmus with widely dilated pupils. The fontanel was not bulging. The neck was not rigid, and Kernig and Brudzinski signs were not elicited. A spinal tap showed 2,300 cells per cubic millimeter, most of which were polymorphonuclears, and a smear showed meningococci. The child died within twelve hours after the onset of symptoms. The condition was fulminating meningococcic meningitis.

DIAGNOSTIC CRITERIA FOR INFANTS AND FOR ADULTS

Josephine B. Neal [12] stated that in many infants meningitis starts as gastro-enteritis with vomiting, slimy green stools and a fever and with or without bulging of the fontanel, and that there are no signs of involvement of the central nervous system, such as Kernig's sign or stiff neck, early in the disease. The doctor who is not aware of this syndrome will treat the condition as gastro-enteritis, and the diagnosis will be made after ten days or two weeks of the disease, when the stiff neck and Kernig sign appear. By this time the disease is far advanced. It should be remembered that meningitis may be present in the first and second years of life when bulging of the fontanel is associated with an irregular fever higher than one would expect from gastro-enteritis and when gastro-enteritis is not responding to the ordinary methods of treatment. Ravid [10] has reported a series of cases in infants in which constipation, vomiting and abdominal pain marked the onset of a meningococcic infection and so obscured the clinical picture that an initial diagnosis of an acute condition within the abdomen, such as intussusception or pyloric stenosis, was made. Abdominal cramps were prominent. There may be bloody stools in cases of the gastro-enteritis accompanying a meningococcic infection, but this symptom is rare. The vomiting is usually nonprojectile, being in infants a regurgitation.

It must be noted that an infection of the upper respiratory tract often precedes meningitis in infancy and that "grip" or an "influenzal" infection at times precedes the meningeal signs in adults. Josephine B. Neal expressed the opinion that this infection or influenza is caused not by the meningococcus but by other organisms, which reduce the resistance of the patient to such an extent that the body succumbs to a superimposed meningococcic infection.

The bulging of the fontanel is a very important sign. It is usually termed a "lump on the head" by the mother. It is an indication that the ventricles are distended with spinal fluid. The examiner should put

12. Neal, Josephine B.: Experience of the Meningitis Division of the New York Department of Health, Am. J. Pub. Health **21**: 147-162 (Feb.) 1931.

the infant in a sitting position to determine whether the fontanel bulges, as when the child is supine the state of the fontanel may be deceiving.

The absence of bulging of the fontanel does not rule out meningitis, as the cranial sutures in infancy are elastic. The increased intracranial pressure may merely serve to separate the cranial bones, without producing a bulging of the fontanel. When the child cries he tends to produce the condition.

If the baby has a petechial rash or a swelling of a joint, one must rule out a meningococcic invasion of the blood stream. The presence of herpes with a fever of obscure origin may mean meningococcemia.

Fretfulness, refusal to nurse or restlessness may herald meningitis. The bright child loses his vivacity. He may be irritable at all times or only when disturbed for examination or feeding. He may be stuporous and difficult to arouse but when he is aroused may manifest irritability.

The patient suffers from acute pain and may complain of generalized soreness. The pain is usually situated in the frontal and occipital regions of the head but may involve also the lower extremities, back or abdomen. It varies in severity throughout the day, being worse at night. When one attempts to flex the neck, an intense cry due to pain in the occipital region is elicited.

*Statistics on Meningococcic Meningitis in Newark, N. J.**

Year	Number of Cases	Number of Deaths	Mortality, Percentage
1918	102	45	44.1
1919	42	22	52.4
1920	29	16	55.2
1921	23	11	47.8
1922	26	16	61.5
1923	20	15	75.0
1924	18	10	55.6
1925	12	8	66.7
1926	16	4	25.0
1927	15	8	53.3
1928	36	14	38.9
1929	66	26	39.4
1930	53	16	30.2
1931	32	9	28.1
1932	10	4	40.0
1933	10	3	30.0
1934	7	2	28.6
1935	8	3	37.5
1936	47	22	46.8
Total number (19 years)	572	254	44.4

* Two striking phenomena about an epidemic are the low morbidity and the high mortality, as contrasted with those for other contagious diseases.

The presence of exaggerated tendon reflexes in a quiet or somnolent patient who is acutely ill or febrile may mean meningitis. Normal infants, excited by the manipulation of examiners and strangers, often show hyperactive reflexes, so these signs must be used in conjunction with other objective phenomena pointing to a cerebral irritation. The deep reflexes may be normal, diminished or exaggerated, no uniform variability being present. The superficial reflexes are of no value. Fever, hyperesthesia and increased reflexes may be the only early signs.

The Kernig sign is very important in the diagnosis of meningitis in adults. It is found in a considerable number of normal infants and may not occur in infants who have cerebrospinal fever. Its absence should not lead one to exclude meningitis; its presence should make one look for other signs.

The Brudzinski sign is important in adults, but it is found in many normal infants. Its presence does not have any significance unless associated with other signs of meningitis.

Tonic spasm of various muscular groups is a constant sign, which, although it does not occur early, is always present during the course of meningitis. Tonic muscle spasm gives rise to the stiff neck, Kernig's sign, Brudzinski sign and cervical and general opisthotonos. Tonic spasm of the upper and lower extremities causes flexion of the arms, legs and thighs, to which the term "gun hammer" has been applied. The extremities may be held in extension. Stiffness of the neck may, as shown by Eagleton be intermittent. Risus sardonicus and trismus have been reported.

A Babinski sign is present normally during infancy and is not characeristic of meningitis. Ravid [10] said that distention of the veins of the neck is a valuable sign. The tache cérébrale is very marked, as in all forms of meningitis.

The onset of a meningococcic infection is usually attended by a moderate or high fever, with a normal or slightly increased respiratory rate. The temperature curve is irregular, the fever having periods of remission or exacerbation. In a remission, the temperature falls to normal, or nearly normal, and remains there for several days. When the patient is seen in this period the condition may be difficult to diagnose. An afebrile period may occur at the beginning of a meningococcic infection and further contribute toward hiding the presence of a febrile illness; fortunately, this occurrence is rare. Some patients never show much fever. According to Herrick,[3] prolongation of fever beyond the seventh day suggests that treatment is inefficient. At that time complications and serum sickness are additional causes for prolongation of the fever. There is nothing characteristic about the relationship between the pulse rate and the temperature. The pulse is usually more rapid than normal, and it is subject to sudden changes in rate; as the intracranial pressure rises a relatively slow rate may appear, and if there is general debility the pulse will be rapid. One does not see the rapid respirations that a patient with pneumonia has. The combination of rapid respirations and meningeal signs usually means pneumonia with meningismus.

Macewen's sign is of no value except when there is distention of one ventricle, when a slightly tympanitic cracked-pot percussion note is elicited over the distended ventricle. This sign is rarely used.

A convulsion in a baby may mean meningitis. It is of no special diagnostic significance, since any febrile disturbance in infancy may produce a convulsion. Instead of a generalized convulsion, localized intermittent tremors and twitchings of an extremity or of one side of the face may occur. The picture may be identical with that of tetany or intracranial hemorrhage in the infant. The combination of convulsions, a hemorrhagic eruption and cyanosis may mean fulminating meningococcemia.

Careful observation of the eyes of a febrile infant may enable one to detect meningitis. One should watch for nystagmus, which occurs early. Nystagmus may occur only on attempted flexion of the head. The ocular movements may be slower than in true nystagmus and involve one eyeball only. If both eyeballs are involved, their movements show dissociation. Strabismus may be present. At times there is ptosis. Retraction of the upper eyelids may be noted. The pupils are

usually contracted early in the disease. Later they may be fixed, dilated or unequal and not respond to the light reflex. The child may appear sightless and have a peculiar stare. Hippus may be present. Ravid [10] stated that purulent conjunctivitis may be the first sign to usher in the disease, but it is usually diagnosed as being of gonorrheal origin, the true aspect manifesting itself only several days afterward. Choked disk may be present, but it is not a frequent or a constant symptom. The papilledema, when it does develop, is due to an internal hydrocephalus. Choking of the disk is therefore a complication and not an early sign in meningitis. The eyegrounds are normal early in the disease and are of no aid in making an early diagnosis.

There is no evidence early in this syndrome of any weakness of the extremities, such as occurs in poliomyelitis. Partial or complete paralysis of an extremity constitutes a complication and occurs late in the course of cerebrospinal fever.

SUMMARY

A thorough knowledge of the bacteriology, anatomy and physiology of the meninges and the cerebrospinal fluid is essential for the proper early diagnosis and treatment of meningococcic infections.

Meningococcic infections have a low incidence and a high mortality. In the city of Newark during the past nineteen years there were 572 cases, with a mortality of 44.4 per cent.

A petechial or purpuric rash may be considered the specific rash of meningococcemia. A purpuric rash accompanies the petechial rash when the condition is fulminating. The rash occurs before the spinal fluid becomes cloudy and before the onset of meningeal signs and persists after definite meningeal signs appear. In many cases meningococci can be demonstrated by a Gram stain of blood obtained by needle puncture of a petechial or purpuric area. A Wright stain of blood from a nonpurpuric skin may also demonstrate meningococci.

Acute fulminating meningococcemia associated with adrenal hemorrhages has been termed the Waterhouse-Friderichsen syndrome.

A meningococcic infection attacked four children in one family, with recovery of two and death of the other two, and postmortem examination revealed the typical pathologic changes in the Waterhouse-Friderichsen syndrome. Cases 3 and 4 of this group illustrate the quick death of the patient, within twenty-four to thirty-six hours after the onset of symptoms. Negative tests of the spinal fluid have been reported in a majority of similar cases.

Three of the cases reported illustrate toxic encephalitis secondary to meningococcic meningitis; in such cases striking deviations from the normal mentality attract the attention of the experienced observer.

Two patients had initial complaints of pain and tenderness in one joint, necessitating a tentative diagnosis of mono-articular arthritis. The stiff neck and Kernig sign did not appear until two days after the onset of arthritic symptoms.

In infancy, particularly in the first and second years of life, the early signs of meningococcic infection of the meninges do not point to involvement of the central nervous system. They are more likely to suggest an infection of the upper respiratory tract or a gastrointestinal disturbance. After the disease is well established, the stiff neck, the Kernig and Brudzinski signs and other meningeal signs appear.

VASCULAR ACCIDENTS OF THE EXTREMITIES

GÉZA DE TAKÁTS, M.D.

CHICAGO

The term vascular accident has not been used in relation to the extremities. It implies, however, that a sudden unexpected change takes place in circulation in the form of hemorrhage, embolism or thrombosis. It also means that emergency measures have to be adopted, the promptness of which may save the limb or the life of the patient. In this brief discussion I plan to outline the types of vascular accidents which occur in the arterial and venous system of the extremities, together with their immediate and delayed treatment.

The general practitioner knows of the accident first in the overwhelming percentage of cases; early recognition and early simple measures may be deciding factors in the ultimate outcome of the emergency.

ARTERIAL HEMORRHAGE

A clean division of an artery, as contrasted with a blunt, crushing injury, is more apt to lead to hemorrhage, since arterial contraction is less effective and blood-clotting substances less abundant in the clean cuts of the arterial wall.[1] Gunshot wounds, stab wounds or fragments of fractured bone are the most frequent causes of massive arterial hemorrhage. If the hemorrhage is external, pouring through a break in the skin, digital compression or constriction above the injury will have to stop the bleeding. However, if bleeding takes place in the soft tissues, with formation of a large hematoma, such bleeding can arrest itself when the pressure of the extravasated blood becomes equal to the pressure within the artery. Such a hemorrhage will frequently result in the occlusion of the vessel except when an aneurysm or a so-called pulsating hematoma develops.[1a]

Severe trauma to large vessels, then, may result in hemorrhage, thrombosis or aneurysm, but in any case the signs and symptoms of vascular impairment must be looked for. Subjectively, numbness, tingling and pain in the bloodless area are the complaints. Motor paralysis is sometimes the first symptom. Objectively, pallor, cyanosis, a drop in the temperature of the skin and loss of pulsation are observed. If nothing is done or nothing can be done to relieve the vascular occlusion, gangrene develops in a certain percentage of cases. An important condition often unrecognized frequently occurs after trauma in the neighborhood of a vessel. A traumatic vessel spasm may so contract a contused artery that it closes completely and organic closure is simulated.[2] The spasm is occasionally indistinguishable from an actual closure of the vessel, and, even if the vessel is closed by a clot, a certain amount of spasm is always present in the collaterals. This is important, as it necessitates special measures to overcome this part of the vascular accident.

Obviously, bleeding must be stopped. Bleeding from a middle-sized or large artery cannot be stopped by

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Read at the annual meeting of the Upper Peninsula Medical Society, Aug. 20, 1937, at Houghton, Mich.

1. de Takáts, Géza: Trauma and Peripheral Vascular Disease, in Brahdy, Leopold, and Kahn, Samuel: Trauma and Disease, Philadelphia, Lea & Febiger, 1937.

1a. No attempt will be made to discuss the surgical treatment of aneurysms. They should not be attacked surgically for several weeks or months after the injury.

2. Montgomery, A. H., and Ireland, Jay: Traumatic Segmental Arterial Spasm, J. A. M. A. **105**: 1741 (Nov. 30) 1935.

packing. Temporary constriction, which should not last longer than from one-half hour to an hour, must be followed by ligation or suture. Ligation of a larger artery must be undertaken with the understanding that, dependent on the site, gangrene follows in a certain percentage of cases. In figure 1 the underlined numbers represent the percentage of gangrene following ligation of the artery at the site indicated, based on the collective statistics of Heidrich. It will be noted that ligation on the upper extremity is much less dangerous and that the risk of gangrene for ligation on the lower extremity is 100 per cent for the aortic and for the common iliac artery, 13 per cent for the external iliac artery, 21 per cent for the common femoral artery, 37 per cent for the popliteal artery and none for the posterior tibial artery.

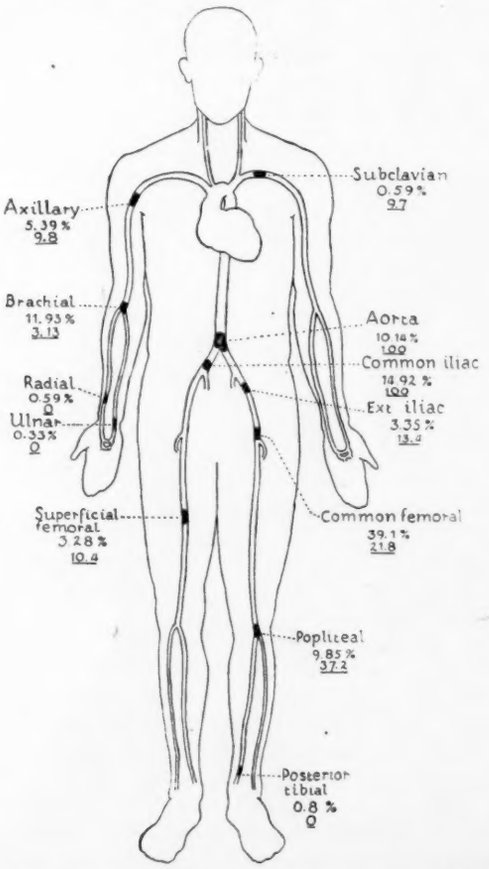

Fig. 1.—Diagram of peripheral arterial occlusions at typical sites. The first figure indicates the incidence of emboli calculated from the collective statistics of Pearse.[7] The figure below it, underlined, represents the percentage of gangrene following ligation of the artery, based on the collective review of Heidrich (cited by de Takáts [5]). Obviously an embolus produces far more embarrassment of circulation than a simple aseptic ligation, chiefly because of the greater probability of superimposed thrombosis. However, the underlined figures give a fair idea concerning the danger that gangrene will follow at a given site.

These are of course only average figures, but they give a fair indication of the risk of tying a large artery. To minimize the erosion of the vessel wall by the ligature or by accompanying infection, the vessel should be doubly ligated and severed. The stumps are then transfixed with a suture ligature, to ensure against slipping. If the distal stump shows pulsation, collateral circulation is abundant. If not, it is wise to tie the concomitant vein, as the increased venous pressure aids circulation temporarily and may tide the limb over the critical period.[3] An extremity whose large artery is ligated needs further care, even if it does not become gangrenous. It is cold, numb and pulseless; the muscles become atrophic; contractures of muscles and tendons may develop, and ischemic neuritis sets in. As soon as the injury is healed all measures known to increase collateral circulation must be employed. These will be discussed later, together with the general therapy of arterial occlusions.

When equipment and previous training enable the surgeon to attempt a suture of the artery, the suture will yield far superior results than ligation. Nobody can have enough opportunity in civilian practice to perfect himself in the technic of arterial sutures, but I would suggest to the younger men that they study it on the experimental animal. Suitable needles and suture material can be kept on hand in ampules. The technic of arterial sutures can be learned by any one who can undertake to suture an injured or perforated bowel, and yet sutures are not done as often as they should be.

ARTERIAL EMBOLISM

When an artery of the extremity is suddenly occluded by a clot which has been thrown off from the heart or from a vessel proximal to the obstruction, one speaks of an arterial embolus. The sources of such emboli are shown in table 1. The main source is the left side of the heart; the mitral stenosis of a rheumatic heart and the myocardial infarct following coronary thrombosis are the two most frequent types of heart disease which are complicated by peripheral embolism. Rarely, a thrombus may break loose from the field of operation and produce an embolus toward the periphery. Figure 1 shows the incidence of emboli at various segments of the arterial tree. The symptoms of sudden arterial occlusion are variable and multiple. The classic description is that of a sudden excruciating pain at the site of the embolus in a patient suffering from heart disease; simultaneously the affected extremity becomes paralyzed, cold and pale, and the pulses disappear. Within a few days the skin becomes mottled, then diffusely cyanotic or gangrenous.

According to my experience pain is not always a prominent symptom, at least not at first; numbness and tingling or motor paralysis may precede the pain by several hours. Furthermore, the pain is not due to an impact of the clot against the vessel wall, but, as Sir Thomas Lewis [4] pointed out, is due to ischemia of the musculature. In some of my cases pain has been entirely absent.

Arterial thrombosis, in contrast, usually comes on gradually. There is often some preexisting evidence of peripheral arterial lesions, such as arteriosclerosis or Buerger's disease, and there is no obvious source of embolism in the heart. Yet it must be emphasized that the differential diagnosis between arterial embolism and thrombosis is sometimes difficult and occasionally impossible.[5] Thus, it has been noticed by several observers that arterial embolism is sometimes not as sudden as the textbooks would have it and that numbness, coldness and tingling may appear days and weeks before the fulminating symptoms. The former are probably due to preliminary showers of the central clot, which is about to break loose. On the other hand, arterial thrombosis, which usually has a gradual onset, may occur so suddenly that it is the first recognized

3. Brooks, Barney; Johnson, G. S., and Kerthey, J. A., Jr.: Simultaneous Vein Ligation: An Experimental Study of Effect of Ligation of Concomitant Vein on Incidence of Gangrene Following Arterial Obstruction, Surg., Gynec. & Obst. **59**: 496 (Sept.) 1934.

4. Lewis, Thomas: Pain as an Early Symptom of Arterial Embolism and Its Causation, Clin. Sc. **2**: 237 (July) 1936.

5. de Takáts, Géza: Acute Arterial Occlusion of the Extremities. Am. J. Surg. **33**: 60 (July) 1936.

symptom of a widespread arterial disease. One sees occasionally popliteal thrombosis in an elderly arteriosclerotic patient or in a juvenile thrombo-angiitic patient which may be mistaken for embolism. The differential diagnosis between arterial embolism and thrombosis has more than academic interest.

In spite of all that has been said recently of various conservative measures to increase circulation when an embolus occludes an artery, the extraction of the clot

TABLE 1.—*The Source of Peripheral Emboli in 296 Cases (Pearse [7])*

	Percentage
Heart disease	69.2
Postoperative states	13.0
Infection and trauma	2.1
Arteriosclerosis	2.1
Aneurysm	1.8
Abortion and delivery	1.8
Miscellaneous	2.8
Phlebitis	0.3

is still the optimal method of treatment. In order to define the indications for an embolectomy, it is well to examine the factors which determine the ultimate fate of a limb affected by acute arterial occlusion. They may be readily grouped under four headings: (1) the condition of the heart, (2) the condition of the vessel wall at the site of obstruction, (3) the condition of the collateral vascular bed and (4) the time elapsed between the early symptoms and effective treatment. Of these four factors, the condition of the heart and of the vessel wall cannot be influenced. There is in fact a danger of aggravating circulation by overanxious digitalization. I have repeatedly learned from our medical staff at St. Luke's Hospital that patients who are indiscriminately digitalized after coronary occlusion are more apt to throw peripheral emboli. Digitalis in the treatment of coronary occlusion is indicated only in the presence of decompensation; it slightly constricts the coronaries and increases muscular contractions. The last two patients with multiple embolism whom I saw were both heavily digitalized after coronary thrombosis.

One can, however, influence the time factor and the state of the collateral vascular bed. In regard to the time factor, the statistics of the Swedish surgeons provide a model example. Key's collective review shows that the medical profession in Sweden has become conscious of the utmost urgency of the situation. Of 213 embolectomies, 135, that is, 63 per cent, were performed within the first ten hours.[6] What that means in regard to results is shown in table 2.[7] In this country Herrmann's [8] latest figures show that of twenty-one patients with acute embolism ten could be treated within the first twelve hours and that of twenty-five patients with thrombosis six, or 30 per cent, were referred for treatment within twelve hours. My material, consisting of a total of fifty patients suffering from sudden arterial occlusion, contains fifteen patients who had arterial embolism; in only five of these could exploration be done, and only two arrived within less than ten hours. It seems that those of us who teach surgery in medical schools have not done our duty to impress the medical profession with the utmost urgency of acute arterial occlusion. The general attitude is that the leg will become gangrenous and the patient will die anyway.

It might be well to state what can be accomplished when the patient is seen in the first ten hours. First one must make an attempt to differentiate between embolism and thrombosis, keeping in mind the possibility of venous thrombosis with arterial spasm, which will be discussed a little later. Then one must try to localize the site of occlusion and determine, on the basis of the patient's age, cardiovascular status and the available collateral bed, whether or not gangrene is to be expected. Gangrene seldom follows an embolus to the upper extremity, and while embolectomies on the upper extremity are uniformly successful, they are unnecessary, for one can get along without them.

Thirdly, intensive conservative measures must be adopted to open up the entire collateral bed and produce as much peripheral vasodilatation as possible. These measures are available to every practitioner, and I have seen limbs saved by a systematic use of peripheral vasodilators. A large heat cradle must be placed over both lower extremities and the abdomen;[9] it can be improvised in any home. The temperature in the cradle need not exceed 90 F. The use of excessive heat to the extremity is harmful, as heat creates an increased demand for oxygen, and that accentuates the arterial deficiency. The limb should not be elevated, as it commonly is, because elevation only decreases arterial inflow; on the contrary, it should be in a dependent position, somewhere between 10 and 15 degrees below the horizontal position. The angle must be so selected that the tips of the extremity regain their normal color.[10] They should be neither pale from too much elevation nor dusky red from too much dependence. Next an intravenous injection of a potent vasodilator is given. Papaverine hydrochloride in one-half grain (0.03 Gm.) doses [11] or sodium nitrite in 1 grain (0.06 Gm.) doses is kept on hand, dissolved in a few cubic centimeters of physiologic solution of sodium chloride or distilled water and boiled in a spoon over a flame just before use. These doses have been so selected that, while the general blood pressure is affected little or not at all,[12] an enlargement of the vascular bed, chiefly the venocapillary part, takes place. This aids circulation and overcomes the initial vasoconstriction, which accompanies all acute vascular occlusions. Obviously the heat and the vasodilators are not going to influence the clot, but they do open up the collateral arterial pathways, which, curiously enough, are in a state of spasm. This spasm is due

TABLE 2.—*Results of Embolectomy (Pearse [7])*

	Percentage Successful *
First ten hours	40
Second ten hours	14
Third ten hours	8
No successful operations after forty-eight hours	

* Success is defined as restoration of circulation for at least one month.

6. Key, E.: Die Embolieoperationen auf Grund der bisherigen Erfahrungen, Ergebn. d. Chir. u. Orthop. **22**: 1, 1929.
7. Pearse, J. E., Jr.: Embolectomy for Arterial Embolism of the Extremities, Ann. Surg. **98**: 17 (July) 1933.
8. Herrmann, L. G.: Experiences with the Conservative Management of Acute Arterial Occlusion, read before American Heart Association, Atlantic City, N. J., June 7, 1937.
9. Lehman, E. P.: A Suggestion for Simple Treatment of Acute Arterial Spasm, Am. J. M. Sc. **190**: 459 (Oct.) 1935.
10. Reid, M. R.: The General Care of Peripheral Vascular Diseases, Ann. Surg. **96**: 733 (Oct.) 1932.
11. de Takáts, Géza: The Use of Papaverine in Acute Arterial Occlusions, J. A. M. A. **106**: 1003 (March 21) 1936.
12. Beck, W. C., and de Takáts, Géza: The Use of Sodium Nitrite for Testing the Flexibility of the Peripheral Vascular Bed, Am. Heart J. **15**: 158 (Feb.) 1938.

partly to fear, pain or shock, following the embolism, but is specially pronounced in the affected extremity as a reflectoric vessel spasm.[5]

When a negative and positive pressure apparatus is available, it also can be applied to the affected extremity. According to my experience, however, these machines are far more helpful at a later stage, when a slow and gradual enlargement of the collateral vascular bed is desirable. In the treatment of acute obstruction, their use has specially been urged by Herrmann,[8] but he said that they act in overcoming the vessel spasm, which may easily be overcome by heat and drugs. Intermittent venous hyperemia has also been found to be useful in the treatment of the late sequelae of acute occlusions.[13]

In a large number of cases, the aforementioned simple measures suffice and the limb regains its normal color and temperature. If this does not happen within an hour after the administration of vasodilators, the limb is headed slowly or rapidly toward gangrene. In communities where the physicians are awake to the great seriousness and urgency of this vascular accident, early treatment may save a number of lives and limbs.

In the small group of cases in which early conservative measures have not brought about an improvement in circulation but in which, on the other hand, the limb is not yet ready for amputation, embolectomy should be attempted. That the results are poor after the first ten hours has already been stated; yet one may save a limb occasionally after twenty-four hours. The reason for the great hurry in removing the clot is not only that muscle and nerve tissue, deprived of arterial blood, will suffer permanent damage but that the obstructing clot continues to grow, chiefly in the form of a descending thrombus, which plugs up collateral vessels and defies the purpose of the late embolectomy. In addition the vessel wall starts a reactive process against the clot and becomes irritated, and when such a vessel wall is sutured thrombosis readily occurs at the suture line.

The embolectomy itself is not difficult when suitable equipment and team work are present. Most frequently the groin and the popliteal fossa are explored with the patient under local anesthesia. Nystrom[14] has shown that clots in the aorta or the common iliac artery may be approached from an incision at the groin and with subperitoneal massage can be brought out through an incision in the femoral artery.

Embolectomy is futile after forty-eight hours or even before that when there is manifest gangrene or when the underlying disease is apt to be fatal within a short time, as are septic endocarditis and terminal cardiac decompensation. It is seldom indicated in the upper extremity.

Recently the impression has gained ground that early conservative measures will make embolectomies unnecessary. The answer to this problem can be found by examining the fate of limbs after embolectomy and after conservative measures. About one half of the patients who have a successful embolectomy within the first ten hours and do not die of the underlying cardiac disease leave the hospital with restored circulation. Strombeck,[15] who published some late results, found that, of such patients, three fourths were alive after one year, half after three years, one third after five years and one eighth after ten years. These are encouraging figures when one realizes how severely handicapped these patients are. Much less is known about the circulation of the extremity that has survived the acute vascular occlusion without gangrene and without embolectomy. I have under observation five patients with such an extremity. In each case it is pulseless and atrophic, the muscles contracted and fibrosed and the skin scaly and mottled. The leg is very painful because of ischemic neuritis, and severe intermittent claudication is present. If there is a demonstrable vessel spasm, the fibrosed artery may be excised or lumbar sympathectomy done to break up the reflex vasoconstriction. While the limb may slowly improve in function, it does not compare with the one from which a clot has been successfully extracted.

When the patient arrives after forty-eight hours, an amputation should not be delayed if there is any chance of saving his life. It takes considerable courage and optimism to urge amputation. The mortality under these conditions is around 50 per cent. I have two patients who have lived over two years after amputation. In each case the leg had to be amputated because of acute arterial occlusion, and the patients bear eloquent testimony as to the value of not giving up the fight too soon. Naturally, moribund patients should not be subjected to any further ordeal.

Mention should be made of multiple peripheral emboli. When they pass from one extremity to another or to the brain, heart, kidney or intestine, the fight has been lost. It must be emphatically stated, however, to physicians who are skeptical of all therapeutic efforts in the treatment of embolism, that the majority of emboli are single for many months, at least, and that patients may lead a useful although physically limited life for many years. Two patients of mine do their own housework; one woman lived for several years and died of multiple sclerosis; one man, who had a cerebral and two peripheral emboli after a myocardial infarct, lives after two years and is capable of moderate activity.

ARTERIAL THROMBOSIS

It has already been mentioned that, although often easily differentiated, thrombosis occasionally is indistinguishable from embolism. Arterial thrombosis may result from mechanical causes, such as pressure from a crutch or a cervical rib, from burns and from frost bites; it may occur during the course of infectious diseases, such as pneumonia, typhoid fever and typhus, and in association with Buerger's disease or arteriosclerosis. With the latter two diseases it may produce the first clinical symptom and appear so suddenly that one is easily led to think of an embolus. Of course all the measures previously outlined for the treatment of acute arterial occlusions, except embolectomy, must be employed. The suture of a vessel which is the site of local thrombosis must invariably lead to renewed thrombus formation. There is, however, another surgical procedure which often improves circulation, that is, excision of the thrombosed vessel. The thrombosed vessel, just like the one which harbors an embolus, maintains a continuous reflectoric vessel spasm, which is responsible for the coldness, numbness, cyanosis and pain of the affected extremity.

While Leriche[16] has advocated excision in the treatment of Buerger's disease and of arteriosclerosis, I feel

13. de Takáts, Géza; Hick, F. K., and Coulter, J. S.: Intermittent Venous Hyperemia in the Treatment of Peripheral Vascular Disease, J. A. M. A. **108**: 1951 (June 5) 1937.

14. Nystrom, Gunnar: Lectures on Embolism and Other Surgical Subjects, Baltimore, Williams & Wilkins Company, 1936.

15. Strombeck, cited by Nystrom.[14]

16. Leriche, René; Fontaine, René, and Dupertuis, S. M.: Arteriectomy with Follow-Up Studies on Seventy-Eight Operations, Surg., Gynec. & Obst. **64**: 149 (Feb. 1) 1937.

that its use is limited to short, well localized segmental clots following trauma or infection. I have recently seen in consultation a young lad who, in falling from a horse on a sharp object, cut his femoral artery, which had to be tied because of massive hemorrhage. Several months later, when admitted to the Research and Educational Hospital, he had a lot of cyanosis and coldness and had lost a few toes. It could easily be demonstrated with the help of sodium nitrite that some of his circulatory impairment was on a vasospastic basis. As the femoral pulse was well palpable in the groin, the arterial segment to be excised was readily demarcated and its removal advised.

Another confusing picture is that of multiple arterial thromboses, which, just because of their multiplicity, simulate embolism. It has been suggested that the clotting mechanism is at fault, although the etiology is entirely obscure.[17] Periarteritis nodosa may also give rise to acute arterial occlusion and may easily be due to an allergic manifestation of a chronic vascular infection. A patient with multiple sclerosis had arterial thrombosis in the popliteal fossa, which resulted in gangrene and amputation. This is interesting in the light of the recent work of Putnam[18] on the etiology of multiple sclerosis.

VENOUS HEMORRHAGE

Aside from those caused by accidental venous puncture, the majority of venous hemorrhages result from previously existing large varicose veins. Patients with large, thin-walled varicose veins are often afraid of this complication, and yet, although the fact is rather amazing, few of these varices ever produce external hemorrhage. The reason is that usually by the time the skin is thinned out and ready to burst, local periphlebitis has formed around the vein, which thickens the wall or may produce thromboses. The varicose vein which is apt to bleed is uninfected and thin walled and shines through the parchment-like skin like a small blue marble. When one recognizes such a vein before or even after it has bled, it is wise to inject it with a mild sclerosing solution, such as a 5 per cent solution of potassium or sodium oleate, and thus prevent hemorrhage.

Loss of blood from a ruptured varix may be considerable, and I have seen a few exsanguinated patients. Usually, well meaning first aid experts put a tourniquet above the bleeding point, which is unnecessary and if not tight enough will only increase venous bleeding. It is enough to elevate the leg high on pillows and apply an even, snug bandage from the toes to above the point of bleeding, in order to control oozing. Secondary infection or ulcer formation rarely follows such an event, because the surrounding skin is normal and will readily heal. Some patients with congenital vascular anomalies, such as arteriovenous fistulas or aneurysms, frequently bleed from small, pinpoint miliary aneurysms in the skin. For these, roentgen therapy or radium offers a good protection against further hemorrhages.

VENOUS THROMBOSIS

The clotting of blood in the veins is a true vascular accident, as it comes on unexpectedly and with symptoms alarming to the patient. On the upper extremity venous thromboses are comparatively rare. There are, however, two typical forms of thromboses in the upper extremities; the first is ascending thrombosis of the cephalic or the basilic vein following the introduction of irritating substances, such as hypertonic salt solution, dextrose or dyes, or blood transfusions. The treatment is rest, elevation and hot fomentations. A breaking loose of the thrombus hardly ever occurs.

Another infrequent but characteristic type of thrombosis is that of the axillary or the subclavian vein. This may be of traumatic origin, following pressure of crutches in the armpits, fractures or dislocations of the humerus, or extirpation of axillary lymph nodes requiring extensive dissection around the skin. A typical but rare picture is subclavian thrombosis following prolonged muscular strain during which the vein is compressed between the costocoracoid fascia, the subclavius muscle and the bony chest wall.[19] The diagnosis of such venous obstruction can be made by the history of a sudden strain followed by swelling and cyanosis, the development of collateral veins and sometimes a palpable clot in the axilla or under the pectoral muscle. The stripping or the excision of the thrombosed segment hastens the development of collaterals. In one of my cases, stripping of the axillary vein hastened the disappearance of edema and abolished some vasomotor phenomena, such as flushing and a burning pain brought on by exercise.[20]

By far the overwhelming majority of venous thromboses occur in the lower extremities. It is convenient to separate them into four groups.

First, the superficial but not varicose vein may be affected. Spontaneous thrombosis of the normal saphenous veins occurs mostly in males. It produces visible and palpable streaks along the inflamed vessel but usually little change in pulse and temperature. The phlebitis may be tubular and ascending or occur in round or oval patches, jumping intact segments of the vein. There is little, if any, swelling of the calf or ankle. The natural course of the disease is slow regression and frequent recurrence. In the majority of cases, typical Buerger's disease later develops, with involvement of the arteries. Other types of segmental phlebitis, which may migrate to the neck, arms or face, include streptococcic, rheumatic and tuberculous forms, but I have seldom seen them.

The second form is thrombosis in varicose veins, which exhibits essentially the same symptoms. There may be, however, much more redness and swelling, and the size of the clots may approach the size of a walnut or even a tangerine. Because of the width of the saphenous vein, massive thrombosis may ascend rapidly from hour to hour toward the groin. In the patchy type of phlebitis, large areas of periphlebitic edema and induration develop, which are painful to the touch, break down easily and form the base of indolent, profusely secreting thrombophlebitic ulcers. Again, the pulse and the temperature may not be affected in spite of the striking inflammatory reaction in and around the vein.

The third form is thrombophlebitis of the deep veins. This presents an entirely different picture. An early sign is a stepladder type of pulse; a rise in temperature is often present but is not characteristic. There may be pain on pressure over the instep or over the calves. The pulses of the foot are diminished as the femoral artery

17. Barker, N. W., and Baker, T. W.: Proliferative Intimitis of the Small Arteries and Veins Associated with Peripheral Neuritis, Livedo Reticularis and Recurring Necrotic Ulcers of the Skin, Ann. Int. Med. **9**: 1134 (Feb.) 1936.

18. Putnam, T. J.: Evidences of Vascular Occlusion in Multiple Sclerosis and Encephalomyelitis, Arch. Neurol. & Psychiat. **37**: 1298 (June) 1937.

19. Matas, Rudolf: On So-Called Primary Axillary Thrombosis Caused by Strain, Am. J. Surg. **24**: 642 (June) 1934.

20. de Takáts, Géza: Reflex Dystrophy of the Extremities, Arch. Surg. **34**: 937 (May) 1937.

contracts because of the irritation of its vasoconstrictors. Later the skin of the toes becomes warmer on the affected side [21] and there is a slight swelling in the groin. All these signs are prodromal, and should the clot remain small or remain localized in the pelvic veins, no further signs develop and the thrombosis is overlooked. Should the clot occupy branches of the hypogastric vein, such as the perivesical, perirectal, periuterine or periprostatic plexuses, edema of the limb will not develop (fig. 2). Frequent micturition, mucous diarrhea and slight swelling of the suprapubic region are signs suggestive of pelvic thrombosis. Only when a clot breaks loose suddenly and produces pulmonary embolism or when, months or years later, atypical varicosities develop on the lower extremities, will it become clear that small short clots in the pelvis, not obstructing the external iliac veins, have been overlooked.

When the thrombophlebitis is typical and fully developed, however, after the prodromal signs or often

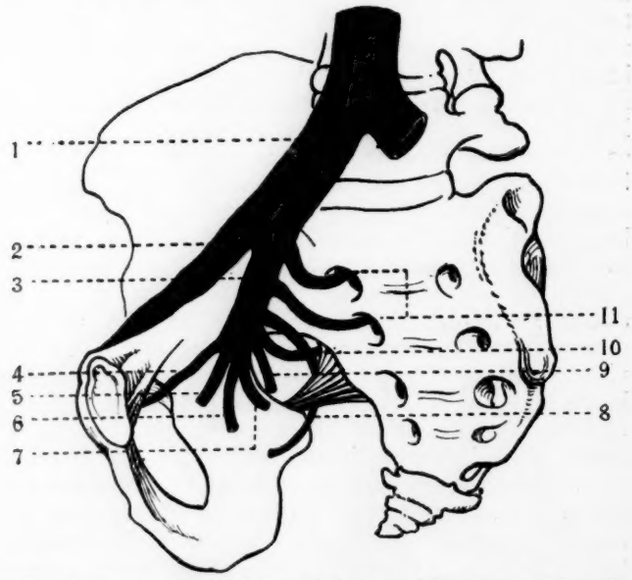

Fig. 2.—The fanwise distribution of the internal iliac (hypogastric) vein in the pelvis. From Ducuing, J.: Phlébites thromboses et embolies postopératoires, Paris, Masson & Cie., 1929, by courtesy of the publishers. The inferior vena cava divides at the upper margin of the sacro-iliac articulation. The internal and external iliac veins unite at a sharp angle. Veins: 1, common iliac; 2, external iliac; 3, hypogastric; 4, obturator; 5, middle vesical; 6, uterine; 7, middle hemorrhoidal; 8, internal pudic; 9, sciatic; 10, gluteal; 11, lateral sacral. Phlebitis of these branches may cause peculiar and simultaneous localizations of edema or abscesses in the vulval, gluteal, sciatic or retrosacral regions.

without them a sudden excruciating pain is felt in the groin, followed by a rapidly increasing swelling of the limb, which is first blue and pits easily on pressure but rapidly becomes white and hard, presenting the so-called milk-leg. The accompanying fever and pain and the general toxic state of the patient diminish the milk secretion of lactating mothers to such an extent that both physicians and the lay public used to think that the milk had wandered down into the legs; hence the name. As Homans [22] has pointed out, this white hard edema is due, at least in part, to blockage of the lymphatics surrounding the large veins and not only to venous edema. The clot becomes palpable along the course of the femoral vein in Scarpa's triangle; it is painful on pressure.

One should add a fourth form of venous thrombosis in the lower extremities, which is fortunately rare but is very often fatal. This is thrombosis of the perforating veins of the muscles in the calf of the leg; it produces localized swelling of the calf, which is painful on pressure, runs a febrile course and often produces fatal pulmonary embolism.[23] The clots in the veins of the muscles grow by apposition, hang into the swift current of the deep veins and are easily mobilized or broken loose by muscular action. All three patients with this type whom I have seen, two of them physicians, have died of pulmonary embolism.

In most cases thrombosis has an infectious basis, and therefore a search must be made for the sources of infection. Infections in teeth, tonsils, prostate or cervix should be eradicated even if an etiologic connection is uncertain, as they may act as sensitizers. Thus, acute recurrent tonsillitis easily reactivates slumbering phlebitis. The removal of foci is best undertaken during a quiescent, chronic stage; a too early search for foci aggravates a latent infection. I have seen fatal pulmonary embolism follow a tonsillectomy undertaken to calm down slowly receding phlebitis.

The superficial type of thrombophlebitis requires elastic support in the form of bandage, stocking, elastic, adhesive tape or a paste of zinc oxide and glycerin. When the patient is seen in the acute stage, roentgen therapy in small doses (from 95 to 100 roentgens with a heavy filter) is given two or three times at ten day intervals. This produces a remarkable regression of the periphlebitic exudate. Rest in bed, elevation of the affected part, hot wet packs or an electric cradle are necessary for only a few days until the fever and pain disappear. Afterward the patient is not immobilized. Prolonged immobilization of patients with the superficial type of phlebitis is not necessary and may even favor the formation of a clot in the femoral vein. Should the thrombophlebitis be tubular, rapidly ascending and accompanied by fever or chills, ligation of the saphenous vein at the saphenofemoral junction is indicated. This prevents further ascent of the clot and beneficially influences the phlebitis by relieving it from fluctuations of pressure coming from above.

In the treatment of deep thrombophlebitis or phlebitis of the communicating veins, one must try to combat (1) embolism, (2) ascending thrombosis and (3) persistent edema. Once the diagnosis of thrombosis in the deep or perforating veins is made, the patient must be immobilized with the limb slightly elevated under a heat cradle. In most cases, first the temperature and then the pulse will return to normal. It has been my custom to wait ten days after the evening pulse has become normal and then to allow sitting up, slight active exercises and a few steps. Should the pulse rate increase again, further immobilization is necessary. The sedimentation rate, if available, is an excellent guide as to the activity of the clot.

In some cases fever persists for many weeks, the white count remains high and secondary anemia develops. In a physician's daughter I saw the development of mild endocarditis, with the production of a murmur. Other patients will show one or two showers of pulmonary emboli. For such patients, especially when they are septic, ligation of the iliac vein above the thrombosis must be seriously considered.[24] In weighing the results of such a ligation, it must be remembered that the venous obstruction is already

21. Ipsen, Johannes: Hauttemperaturen, Copenhagen, Levin and Munksgaard, 1936.

22. Homans, John: Thrombophlebitis of the Lower Extremities, Ann. Surg. **87**: 641 (May) 1928.

23. Homans, John: Thrombosis of the Deep Veins of the Lower Leg, Causing Embolism, New England J. Med. **221**: 993 (Nov. 29) 1934.

24. Bancroft, F. W.: Proximal Ligation and Excision of Veins for Septic Phlebitis, Ann. Surg. **106**: 308 (Aug.) 1937. Neuhof, M.: Excision of Vein for Suppurative Thrombophlebitis, Ann. Surg. **106**: 311 (Aug.) 1937.

present and that the additional ligation will not add to the venous embarrassment if important venous collaterals are avoided. When treatment is successful, the temperature promptly drops and the danger of embolism is minimized.

The next consideration is the emergency treatment of pulmonary embolism, which occurs comparatively infrequently in cases of massive thrombophlebitic edema when the condition is recognized and the patient immobilized, but much more often in association with unrecognized pelvic clots or thrombosis in the perforating veins of the calf. Patients die as a result of a massive pulmonary embolus in a few seconds, in several hours or in several days. Roughly 50 per cent of all patients die before any medical or nursing help can arrive; but the other half live at least fifteen minutes. In some instances an extraction of the clot has been attempted, and of over 100 such attempts, nine were successful.[25] The three great handicaps in the performance of successful operations are (1) the confusion of pulmonary embolism with coronary thrombosis, (2) the absence of a properly trained and equipped surgical team in most communities and (3) the recurrence of pulmonary embolism after a successful embolectomy. The operation at present is to be regarded as an interesting, desperate effort or a stunt, and its wide adoption is not to be expected. More important are some simple measures, which can be used even in the home. If the patient is cyanotic, oxygen should be administered by mask or, better, by an intranasal catheter. One-half grain (0.03 Gm.) of papaverine, as in the treatment of embolism of the peripheral arteries, overcomes the accompanying vessel spasm. If the blood pressure has fallen to 90 mm. of mercury or below, its cautious elevation with ephedrine or neosynephrine may be tried. Too sudden elevation may press more clots through from the right side of the heart, although this is a theoretical consideration.

Should the embolus be small and the patient recover from the immediate danger, bloody sputum, a pleural friction rib and a roentgenogram of the chest will indicate the size and location of the infarct. The best treatment is prevention of further emboli. This is the time, if the location of the original thrombus is recognized, for a prophylactic ligation proximal to the clot.

The last but practically very important consideration is the prevention of future persistent edema of the leg afflicted by deep venous thrombosis. The treatment must really begin on the day of the formation of the clot. Every effort must be made to rid the limb of the swelling, as persistent edema, rich in protein, will produce permanent fibrosis of the subcutaneous tissue.[26] To this end, fluids are restricted to 1,000 cc. a day, salt is restricted and ammonium chloride or nitrate is given in 15 grain (1 Gm.) doses four times a day. The limb is maximally elevated and a heat cradle is applied. Two or three days later a mercury diuretic such as salyrgan is given intravenously, not more than 0.5 cc. at first and 1 cc. two days later. The intravenous administration of calcium gluconate has also proved helpful.[27] All these drugs tend to mobilize fluid from the edematous limb, and if the edema subsides it is much easier to prevent further swelling by elastic support than if the patient is allowed to get up with a swollen limb. After the patient gets out of bed, elastic support must be maintained for a year or longer. Even so, a lasting reduction of the swelling cannot be predicted or promised, as it will depend on the length of the clot and on the extent to which the tributary veins are plugged.

This emergency treatment of deep venous obstruction is again in the hands of the general practitioner. When the patient is seen years after onset, the fluid has become fixed, the lymphatics are destroyed and the tissue is fibrous. At that stage only extensive excision of the diseased tissue can help, but this is to be undertaken only in cases of extreme involvement, in which stasis of lymph predominates.

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26. de Takáts, Géza: The Management of Acute Thrombophlebitic Edema, J. A. M. A. **100**: 34 (Jan. 7) 1933.
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SUMMARY

The first aid given for vascular accidents of the extremities, such as arterial hemorrhage, embolism and thrombosis and venous hemorrhage and thrombosis, will often determine the future course and the recovery or disability of the affected limb. With simple measures available to every physician, the majority of accidents can be adequately handled. In larger communities, the younger surgeons can prepare themselves for the surgical treatment of these emergencies, which often consists of limb-saving or life-saving measures.

122 South Michigan Avenue.

THE EFFECT OF VITAMIN B_1 ON THE PERIPHERAL NEURITIS OF PELLAGRA

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Pellagra has come to be accepted as a clinical syndrome characterized by symptoms referable to the alimentary tract and the dermal and neural systems. The literature on the mental changes in pellagra is extensive, but relatively few observations have been reported on the involvement of the peripheral nerves. While studying so-called alcoholic pellagra a number of years ago, Spies and DeWolf [1] were forced to the conclusion that alcohol is not the sole cause of the neuritis accompanying this disease. The correctness of this point of view has been established by Strauss,[2] Jolliffe, Colbert and Joffe,[3] Spies and Blankenhorn,[4] Romano [5] and Goodhart and Jolliffe.[6]

During our studies on the peripheral neuritis associated with pellagra we noted that we could not distinguish it from the peripheral neuritis of beriberi. This observation led us to administer large amounts of yeast, wheat germ and liver extract to patients with

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3. Jolliffe, Norman; Colbert, C. N., and Joffe, Philip: Observations on the Etiologic Relationship of Vitamin B (B_1) to Polyneuritis in the Alcohol Addict, Am. J. M. Sc. **191**: 515 (April) 1936.
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5. Romano, John: Deficiency Syndromes Associated with Chronic Alcoholism: A Clinical Study, Am. J. M. Sc. **194**: 645 (Nov.) 1937.
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deficiency diseases and accompanying neuritis. Having obtained successful results with this method of therapy, we undertook controlled studies, using crystalline vitamin B_1. These studies form the basis of the present report.

MATERIAL AND METHODS

Six cases of classic pellagra were selected for the study of peripheral neuritis. In four, pellagra had developed after the substitution of the calories of alcohol for the calories ordinarily obtained from food. In the remaining two cases the pellagra was unassociated with chronic alcoholic addiction (the so-called endemic type of pellagra). It has been pointed out previously [4] that the severe peripheral neuritis associated with pellagra usually progresses when the patient is restricted to a pellagra-producing diet. The vitamin B_1 crystals (aneurin, torulin, thiamin) given as supplements to the pellagra-producing diet used in this study were supplied through Dr. Hans Molitor of Merck & Co. Histories of two representative cases of pellagra with involvement of the nerves follow:

CASE 1.—*History.*—G. S., a Negro woman, aged 34, was admitted to the medical service of the Cincinnati General Hospital on Dec. 7, 1937. About ten months previously her husband had gone "on relief," which made it necessary for five adults, including the patient, to subsist on $6 a week. Three months before the patient's admission to the hospital her appetite became very poor, and a month later she began to note numbness, pain and tingling in the feet and legs. Her tongue became sore at about this time. One month before her admission a scaly, dry and symmetrical eruption appeared over the dorsa of both hands. One week later the same type of dermal lesion developed beneath the breasts and about the vagina, and the lesions on the hands spread to involve the flexor and radial surfaces of the forearms up to the elbows.

At about this time the patient's physician prescribed a diet consisting of milk, greens and an occasional egg and told her to eat no meat. She lost weight rapidly on this regimen. Shortly thereafter numbness was observed in the upper extremities and the trunk. December 3 she lost consciousness for about two hours. On regaining consciousness, she was delirious, salivated profusely and apparently could not move her lower extremities. Thereafter she continued to salivate profusely, was apprehensive and weak and complained of soreness of the mouth.

The past history contained nothing related to her condition at the time of admission to the hospital, with the single exception that she had partaken moderately of alcoholic beverages and had occasionally overindulged. However, she had not done so within three or four years prior to admission.

Examination.—There were dark, dry, scaly lesions, symmetrical and well demarcated, on the dorsa of both hands, along the flexor and radial surfaces of the forearms and over the elbows. The same type of lesion was present beneath the breasts, in the skin of the perineum, in the sacral region, over the dorsa of the feet and about the ankles. The lesions beneath the breasts were macerated and reddened and exuded serum. The tongue was smooth and scarlet, and the entire buccal membrane was very red, as were the margins of the gums. The gums were partially covered by a thick Vincent's membrane. The openings of Stensen's ducts were enlarged and reddened. The lips were swollen and cracked. The patient was salivating profusely. The blood pressure was 98 systolic, 60 diastolic.

Neurologically she presented several abnormalities. She was dull and could not concentrate or cooperate for any length of time, her responses were unreliable, and she was very apprehensive and occasionally became excited. There were mild wasting of the muscles in the gastrocnemius group in the legs, tenderness in the muscles of the lower extremities and diminution in the perception of touch, pain and temperature below the knees. All of the tendon reflexes were very active with the exception of the ankle jerks, which could not be elicited. Left patellar clonus was present.

The blood count showed 3,500,000 red cells, which were normal in size and color. The hemoglobin content was 11 Gm. per hundred cubic centimeters. The white cells ranged between 4,200 and 8,200, with a normal differential count. Examinations of the urine and the stools gave normal results, except that large quantities of coproporphyrin were excreted in the urine. The excretion returned to normal after the administration of nicotinic acid. The carbon dioxide-combining power was 43 volumes per cent. The blood urea nitrogen content was 9 mg. and the serum protein content 5.9 Gm. per hundred cubic centimeters. The Wassermann reaction of the blood was positive on one occasion and negative on two others. The Kahn reaction of the blood was positive, with sensitized antigen, on three occasions. Myriads of Vincent's organisms were demonstrated in smears from the gums, the vagina and beneath the breasts.

Progress.—On admission (Dec. 7, 1937), the patient was placed on a pellagra-producing diet. This diet included corn meal, hominy, white flour, sugar, pork fat, sweet potatoes and small amounts of cabbage and collards. It resembles Goldberger's and Wheeler's diets more than any of the other deficient diets; the total calories are adequate, the protein is low and the minerals (calcium, phosphorus and iron) are low. It is adequate in its vitamin A and C content but low in vitamins B, D and G.

On December 7, 500 mg. of nicotine acid was given orally in doses of 100 mg. every half hour. Transitory itching of the dorsa of the hands and wrists followed. Thereafter 1 Gm. of nicotinic acid in a 1 to 1,000 solution was administered daily until the patient's discharge from the hospital (200 cc. of the solution orally five times a day). On December 8 the buccal mucous membranes were less red. Stensen's ducts were not as prominent as they had been at the time of admission, and the salivary secretion, of which the patient expectorated 2,000 cc. during the first twenty-four hours in the hospital, dropped to 50 cc. of expectoration within forty-eight hours. The mucous membranes of the oral cavity and the vagina healed within twenty-four hours after the nicotinic acid therapy was begun, but the dermal lesions healed slowly and the peripheral neuritis became worse, in that the spontaneous pain, the numbness and the pain caused by handling the feet were much more severe. The intravenous injection of 10 cc. of sterile saline solution for three days, beginning December 14, did not have any therapeutic effect (suggestion). By this time Vincent's organisms had disappeared from the mouth, vagina and lesions of the skin.

On December 17 and daily thereafter 50 mg. of crystalline vitamin B_1 in sterile physiologic solution of sodium chloride was injected intravenously. The diet was not altered. On December 19 the patient volunteered that the pain and numbness in the legs had disappeared, and her appetite became vociferous. She complained of having too little to eat, though she was given the basic diet. She became cheerful and lost apprehension, she was alert and her responses to sensory tests were accurate for the first time. There was no change in the other results of neurologic examination, except that muscular tenderness in the lower extremities was obviously diminished. Her weight, which was 123 pounds (56 Kg.) on December 12, had increased to 131½ pounds (59.6 Kg.) by December 18. On December 22 she was able to get out of bed for the first time since admission, and she walked without difficulty. On December 26 her weight was 141½ pounds (64.2 Kg.). She was given a well balanced diet for a few days prior to discharge. She was discharged from the hospital much improved on December 29. The dermal lesions of the hands and forearms had disappeared, and those beneath the breasts and about the perineum had healed, leaving only residual pigmentation.

CASE 2.—*History.*—C. S., a white man, aged 52, was admitted to the medical service of the Cincinnati General Hospital on Oct. 27, 1937. Since April 1937 his regular diet had been gradually replaced by whisky, so that by May 1937 he was consuming from 1 to 2 pints daily. In mid-June dermatitis appeared on the dorsa of the hands and on the elbows. Two weeks later these areas were reddened, tough and blistered. At this time the patient's tongue became sore and very red, and shortly thereafter pains in the legs, which radiated down to the toes, developed.

On July 13 he entered the St. Elizabeth Hospital, Covington, Ky., where a diagnosis of pellagra and polyneuritis was made. We saw him there. Six ounces (180 cc.) of dry powdered brewers' yeast was administered each day, and at the end of two weeks his dermal lesions began to recede, but severe diarrhea (fifteen stools daily) developed, which lasted for two weeks. The diarrhea, dermatitis and glossitis were finally relieved by the therapy, and he was discharged on August 24. However, the radiating pains in the legs and feet steadily became worse, and by mid-August he could not bear the weight of bedclothes on his lower extremities. In early September the pain no longer radiated; it became constant and was confined to the knees, legs and feet. There was an intense burning sensation on the soles of the feet.

Examination.—The examination performed when the patient was admitted to the Cincinnati General Hospital, on October 27, showed that he was poorly nourished, the tongue was coated and the skin on the dorsa of the hands and elbows presented residual changes of pellagrous dermatitis. The blood pressure was 118 systolic, 80 diastolic.

Neurologic examination revealed that there were six or seven nystagmoid jerks when the patient fixed his eyes to the right or left, the tongue was tremulous and there was some muscular atrophy in the interosseous and the lumbrical muscles, in the thenar and the hypothenar eminences of both hands and in the thigh muscles. The hand grasps were moderately weak, but no other loss of motor power was demonstrable. There was marked tenderness to deep pressure in the muscles of the feet, legs, forearms and arms. The recognition of pain, temperature and touch stimuli was diminished in the lower extremities up to a point about 3 inches above the knees and in the upper extremities up to the insertion of the deltoid muscle. This border was not a sharp one. The appreciation of vibration was diminished about one half in the extremities and even more so in the lower extremities. Fine passive changes in the position of the toes were not appreciated by the patient; however, he named large displacements properly. He was extremely sensitive to stroking of the soles of the feet. The tendon reflexes were normal with the exception of the ankle jerks, which were not obtained. The plantar responses were normal in the right foot; there was no response to plantar stimulation in the left foot.

The blood count showed 5,000,000 red blood cells, which were normal in size and shape. The hemoglobin content varied from 13.8 to 15.6 Gm. per hundred cubic centimeters. The white cells ranged from 6,400 to 9,600, with normal differential counts. The sedimentation rate was 16 mm. an hour (corrected rate). The Wassermann and the Kahn reaction of the blood were positive. Gastric analysis showed no free hydrochloric acid before or sixty minutes after the injection of 1/22 grain (0.003 Gm.) of histamine. The pressure of the cerebrospinal fluid was normal; there were 2 lymphocytes in a blood tinged (trauma) fluid. The total protein content was 72 mg. per hundred cubic centimeters and the chlorides 701 mg. The Wassermann reaction of the cerebrospinal fluid was negative.

Progress.—On October 30 the patient was placed on a basic diet low in vitamin B and on November 3 on the basic diet used in case 1. From November 3 through November 8 he was given small amounts of physiologic solution of sodium chloride intravenously (for its suggestive effect), but he noted that this medicine was "not so good," as he had constant pain and burning sensations in his legs. By November 9 weakness had progressed to such an extent that movements about both ankles were very weak, the left ankle being worse than the right. Flexion and extension of the forearms were definitely weak. From November 9 through December 3 he was given a daily intravenous injection of 50 mg. of crystalline vitamin B_1, receiving twenty-five injections in all. On December 10 he ceased complaining of pain, and by the eleventh he volunteered that there was complete remission of spontaneous pain. On December 14 he walked with ease and without pain for the first time since admission. Whereas salicylates, aminopyrine, barbital and 2½ grains (0.02 Gm.) of codeine daily had been necessary to control the pain before the use of crystalline vitamin B_1, no analgesic was required as long as administration of the vitamin was continued.

The neurologic status was checked daily, and on December 13 the significant observation was diminution of motor power in all the muscle groups of the extremities, more obvious in the distal structures and greater in the lower left extremity than in the right. Only the slighest movement was possible in the left toes and the left ankle. There was diminution of all types of sensation in the distal portions of the extremities, and sensation gradually (no sharp border) approached normal just above the patella and the elbow. Touch was not appreciated in the lower third of the left leg or in the left foot, and the patient was unable to identify pin prick in the left leg until the upper border of the patella had been reached, although he realized that there was "something dull" in the leg when it was stimulated below that level. The same phenomenon was present in the right leg, where the level of identification of pin prick was at the junction of the upper third with the lower two thirds of the leg. The appreciation of vibration was diminished about one half over the malleoli. Position sense was poor in the left toes but good in the right. There was tenderness to pressure in the muscles of the feet, legs and arms, especially over the nerve trunks. There was no complaint of spontaneous pain. The only abnormal tendon reflexes were hypo-active knee jerks, and the ankle jerks were not elicited. It was noted from the neurologic examinations that there was no improvement, with the single exception of the remission of spontaneous pain.

The patient continued to improve, even though the injection of vitamin B_1 was discontinued on December 3. His weight increased and his motor power slowly improved. However, on December 24 he complained of some pain in the axillae, and examination of these regions revealed tenderness about the brachial plexus. In late December and early January spontaneous pain increased and was worse in the upper than in the lower extremities. Sharp radiating pain traveled from the axillae down the arms and into the forearms, and down the posterior surface of the thighs and legs to the feet. By January 3 the motor status had regressed to that noted on December 13, and the patient was extremely tender along the course of the nerves in the axillae, arms and forearms. His weight had improved from 107½ pounds (48.8 Kg.) on November 7 to 116 pounds (52.6 Kg.) on January 1.

COMMENT

The experience detailed in these two cases was similar to that in the remaining four. Irrespective of whether the pellagra followed long-standing ingestion of alcohol, the prompt relief of the spontaneous pain of neuritis by the intravenous injection of crystalline vitamin B_1 was striking in all cases. Nicotinic acid by mouth was used in three cases and completely relieved the severe stomatitis and glossitis and promptly produced healing of all the lesions of the mucous membranes. The observations suggest that the painful peripheral neuritis in these particular cases was caused, at least in part, by a lack of vitamin B_1. The response following the injection of this substance was prompt and dramatic. These studies complement the suggestion offered a number of years ago that the clinical manifestations of the pellagra syndrome are perhaps caused by a lack of more than one essential substance. Not all persons with pellagra, however, have peripheral neuritis.

While these pellagrins responded to a basic diet plus supplements of nicotinic acid and thiamin (vitamin B_1), it is not recommended that such a diet be used in the treatment of pellagra.

SUMMARY AND CONCLUSIONS

1. Our observations suggest that vitamin B_1 deficiency had a role in the development of the clinical manifestations of peripheral neuritis associated with the pellagra in these cases.

2. Certain patients fail to absorb vitamin B_1 effectively by mouth, and it is imperative that they be

given parenteral injections. Parenteral injections shorten convalescence and are desirable from the standpoint of prompt relief of pain.

3. Vitamin B_1 does not cure the glossitis and the stomatitis of pellagra,[7] but the observations in case 1 and in other cases suggest that nicotinic acid, which does cure these symptoms,[8] will not cure the peripheral neuritis.

THE TREATMENT OF METASTATIC CARCINOMA OF THE NECK

SECONDARY TO CARCINOMA OF THE LIP

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My purpose in this paper is to present rather briefly what appears to be the best treatment for metastases to the neck from carcinoma of the lip.

Results obtained by the irradiation of cervical metastases have been reported by Schreiner and Mattick,[1] Schreiner and Simpson,[2] Dund and Holton [3] and others. The diagnosis of cervical metastases in these cases was made clinically. The question always arises in one's mind as to how many of these patients would have had microscopically negative glands. This number would probably vary widely in different series. Bloodgood [4] has stated that he found the clinical diagnosis of metastasis proved wrong much more frequently than the reverse.

Results obtained by surgical intervention have been reported by Fischel,[5] Wangensteen and Randall,[6] Eggers [7] and Kennedy.[8] Glands removed were examined microscopically. It is difficult, however, to classify and compare cases clinically. Different conceptions are had concerning what constitutes a neck clinically negative for metastases, what patients have glands which clinically show only inflammatory hyperplasia, what patients have glands which clinically show metastases, and lastly what constitutes the limit of operability.

Results from the combined irradiation and surgical treatment have been reported by Quick,[9] Martin,[10] Hyndman [11] and Scott.[12] Results are the best, I believe, from this type of treatment. This is the type of treatment advocated in this paper. It has been my observation that one is less biased in one's selection of the method of treatment to be followed in a particular case when all methods are equally available and that better judgment can usually be exercised by one familiar with the various methods of treatment.

Broders [13] has shown a definite relationship between the histology of the lesion and the results obtained by treatment.

An interesting study has been made by Pflueger,[14] reporting the type of treatment given by thirty prominent radiologists, dermatologists and surgeons. Because of the difficulties mentioned, it is difficult to compare the results obtained by these various men and their methods of treatment.

In my opinion the neck should not ordinarily be treated until the primary lesion has been treated and controlled. The primary lesion may be successfully treated, in a very high percentage of cases, by surgery, radium or x-rays. Good surgery is better than poor irradiation, and vice versa. Some lesions, however, are better treated by irradiation, others by surgery. Very briefly, anaplastic tumors of grade 3 or 4 malignancy are more suitable for irradiation. The agent employed is less important in more differentiated tumors of low grade malignancy. As in the treatment of all other tumors, there is a necessity for familiarity with exactly what can be accomplished by both surgery and irradiation. It has become my custom, in order to avoid delay in treating the neck, when operable metastatic glands are present, to excise the lesion of the lip and about two weeks later do a dissection of the neck.

It is generally agreed that cancer metastasis is an embolic phenomenon and that carcinoma cells cannot be demonstrated in the lymphatics or other tissues between the primary lesion and the metastases.

Numerous reports have shown that in carcinoma of the lip remote metastases occur in less than 1 per cent of the cases, and metastasis to the regional lymphatics in from 20 to 25 per cent of the cases.

Lesions most apt to metastasize are (1) those of high grade malignancy, especially grades 3 and 4, (2) infiltrating tumors (papillary lesions are less likely to metastasize), (3) rapidly growing lesions, and (4) previously treated lesions, especially those improperly and inadequately treated. It has been observed that the incidence of cervical metastasis is higher in lesions previously treated with paste or other types of escharotics.

Prophylactic irradiation is not given to the neck. Nodes that are thought to be inflammatory are watched. If there is much doubt or if the nodes are thought to be metastatic, dissection of the neck is done. Preoperative irradiation is not given. Postoperative irradiation (from 3,000 to 4,000 roentgens through two portals) is given in all cases in which the glands removed show carcinoma microscopically. The reason for giving postoperative irradiation is that it is believed, although it has not been proved, that any persistent cells are more sensitive for a short time following surgery. This opinion was recently expressed

7. Spies, T. D.: Unpublished observations.

8. Spies, T. D.; Cooper, Clark, and Blankenhorn, M. A.: The Use of Nicotinic Acid in the Treatment of Human Pellagra, read before the Central Society for Clinical Research, Chicago, Nov. 5, 1937.

From the Tumor Service of the Veterans Administration Facility.

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11. Hyndman, O. R.: Carcinoma of Lip: Clinicopathologic Analysis of Seventy-Seven Cases and Suggestions for Rational Plan of Treatment, Arch. Surg. **27:** 250-266 (Aug.) 1933.

12. Scott, R. K.: Treatment of Epitheliomatous Glands of Neck, M. J. Australia **2:** 505-512 (Oct. 24) 1931.

13. Broders, A. C.: Squamous Cell Epithelioma of Lip, J. A. M. A. **74:** 656 (March 6) 1920.

14. Pflueger, O. H.: Treatment of Neck Glands in Cancer of Lip, Tongue and Mouth; Study of Present Day Practice, California & West. Med. **39:** 391-397 (Dec.) 1933.

by Sir Lenthal Cheatle [15] of London, England, in discussing carcinoma of the breast. Dr. Cheatle also recommends washing out the wound at the completion of the operation with 1:500 solution of mercury bichloride, as he believes that this is likely to destroy any loose tumor cells.

I find no definite proof of the value of irradiation when given prophylactically to the neck or when given when the nodes are palpably enlarged. If the nodes disappear, there is no microscopic evidence that the nodes were metastatic. It has been my observation that true cervical metastasis, microscopically proved, developing from differentiated carcinoma of the lip, is seldom, if ever, cured by external irradiation, either radium or x-rays, and only rarely by a combination of external and interstitial irradiation.

Far advanced, inoperable cases are suitably treated by external irradiation first, and then interstitial irradiation, usually by means of gold implants of radon.

It is not always possible to differentiate, clinically, between hyperplastic inflammatory glands and metastatic glands. It is believed, however, that the number of errors decreases with the experience of the examiner and the carefulness of his examination. It is better to err by removing some nonmalignant glands than to defer surgical operation for observation of the patient, especially if the patient cannot be watched closely.

There are many types of so-called neck dissections. Some men mean merely removal of the gland involved; others, block removal of all lymphatics, from the clavicle to the base of the skull, including the sternomastoid muscle, internal jugular vein and other of the soft tissue structures on one or both sides; some do a complete neck dissection on one side and a partial or upper neck dissection on the other side.

It seems to be the consensus of the best opinion that in carcinoma of the lip, with operable metastasis in the submaxillary or submental nodes, suprahyoid dissection is sufficient. Hyndman [11] believes that dissection should always be bilateral, because of the frequency, in his opinion, of crossed metastasis. Quick [16] states that removal of the submental, submaxillary and upper deep cervical glands, on the involved side, gives as good results as the more radical operations. It has been my custom to follow the latter procedure except

TABLE 1.—*Ten Cases of Carcinoma (Squamous Cell, Keratinizing) of the Lip: No Evidence Clinically of Metastases in the Neck*

Case No.	Date	Name	Primary Lesion	Pre-operative Irradiation	Type of Operation	Glands Microscopically	Post-operative Irradiation	Result
1	7/24/34	R. K.	Advanced grade 2	Yes	Bilateral suprahyoid	Negative	Yes	Well October 1937
2	1/23/35	W. H.	Left lip, 2 by 3 cm.	Yes	Bilateral suprahyoid	Negative	No	Well October 1937
3	2/14/35	D. H.	Right, 2 cm.	Yes	Bilateral suprahyoid	Negative	No	Well October 1937
4	2/18/35	R. G.	1.5 cm. grade 2	No	Right submaxillary node excised	Negative	No	Well October 1937
5	3/25/35	W. R. B.	2 by 3 cm.	No	Bilateral suprahyoid	Negative	No	Well October 1937
6	4/ 7/35	E. A. L.	2 cm., right	No	Bilateral suprahyoid	Negative	No	Well October 1937
7	4/ 9/35	T. J. M.	1 cm., left	No	Bilateral suprahyoid	Negative	No	Well October 1937
8	4/20/35	B. S.	2 cm. grade 3	No	Bilateral suprahyoid	Negative	No	Well October 1937
9	5/ 8/35	E. E. D.	1 cm. left, superficial	No	Bilateral suprahyoid	Negative	No	Well October 1937
10	5/15/35	F. B.	Papillary, 1 cm. grade 2	No	Bilateral suprahyoid and left upper cervical	Negative	No	Well October 1937

In these ten cases, in which the neck was clinically negative for metastases, the glands were microscopically negative in all ten cases. It is believed that operation was unnecessary in these cases. All the patients are living and well.

TABLE 2.—*Fifteen Cases of Carcinoma (Squamous Cell, Keratinizing) of the Lip: Clinical Evidence of Early, Operable, Metastases in the Neck*

Case No.	Date	Name	Primary Lesion	Neck	Type of Operation	Glands Microscopically	Post-operative Irradiation	Result
1	11/24/34	M. S.	Treated for 10 yrs.	Hard right submaxillary	Bilateral suprahyoid	Positive	Yes	Well October 1937
2	1/29/35	L. A.	Recurrent	Hard right submaxillary	Right submaxillary node excised	Negative	No	Well December 1936
3	2/13/35	G. L. F.	Right 2 cm., grade 2	Firm right submaxillary	Bilateral suprahyoid	Negative	No	Well October 1937
4	3/ 8/35	F. B.	3 cm. 3 yrs., midline, grade 3	Hard submental and left submaxillary	Bilateral suprahyoid	Positive bilateral	Yes	Well October 1937
5	4/26/35	P. R.	1 cm. right 2 yrs., grade 2-3	Hard right submaxillary	Bilateral suprahyoid	Positive right	Yes	Well January 1936
6	11/22/35	C. H.	1.5 cm. right, grade 2-3	Hard right submaxillary	Bilateral suprahyoid	Positive right	Yes	Well October 1937
7	6/ 1/36	D. C.	1 cm. right, recurrent, grade 1-2	Submental, small, firm	Bilateral suprahyoid	Negative	No	Well October 1937
8	7/ 3/36	W. B.	Right side, grade 2	Right submaxillary, rather soft	Right submaxillary node excised	Negative, frozen section; positive fixed prep.	Yes	Well October 1937
9	7/26/36	W. B.	Entire lip, 7 cm., grade 2-3	Right submaxillary, hard, 1.5 cm.	Bilateral suprahyoid	Positive	Yes	Well October 1937
10	10/ 1/36	E. L.	Entire lip	Hard submental, 2 cm. left	Left suprahyoid	Positive	Yes	Well October 1937
11	10/13/36	W. B.	Midline lip	Hard submental, 1 cm. left	Submental dissection	Negative	No	Well October 1937
12	2/ 3/37	J. P.	Previous treatment caustics and radium; midline, ulcer 1 cm.; erythema	Submaxillary, bilateral, 2 cm., hard	Bilateral upper neck (2 stages)	Positive, bilateral	Yes	Well October 1937
13	4/ 7/37	G. W. S.	Left 1.5 cm., indurated, ulcerated	Submaxillary, bilateral, 2 cm., hard	Bilateral upper neck (2 stages)	Positive, bilateral	Yes	Well October 1937
14	7/14/37	R. D. B.	Midline 1 cm., indurated, not ulcerated, treated March 1937	Submaxillary, 2 cm., right, hard	Right suprahyoid	Positive	Yes	Well October 1937
15	8/ 6/37	G. A. P.	12 mm. midline, ulcerated, treated June 1936	Submental, hard, 3 cm.	Bilateral suprahyoid (1 stage)	Positive	Yes	Well October 1937

In these fifteen cases, in which there were early operable glands clinically, the glands were microscopically positive in eleven cases, negative in four cases. All the patients are living and well. It is believed that operation was justified and indicated in these cases.

15. Cheatle, Sir Lenthal: Carcinoma of the Breast, presented at Michael Reese Post Graduate Tumor Clinic, Chicago, in September 1936.

16. Quick, Douglas: Radium in Treatment of Metastatic Epidermoid Carcinoma of Cervical Lymph Nodes, Am. J. Roentgenol. **33**: 677-681 (May) 1935.

when the lip lesion is located near the midline or when the lesion is very large or of a highly malignant character. Then, a bilateral suprahyoid and upper deep cervical dissection is carried out. Quick [16] also states that "it is our belief that as satisfactory and successful an operation could be done after a node became palpable as before." This also is my opinion. When metastases occur in the deep cervical glands, a complete neck dissection on the affected side is recommended, saving the internal jugular vein and sternomastoid muscle, unless infiltrated by the growth. An upper neck dissection may, or may not, be done on the opposite side. Bilateral complete neck dissection is seldom indicated.

As a general principle, it is believed that dissection should include not only the anatomic triangle involved but also the two triangles bordering it; that is, the one on each side. For example, for metastasis in the right submaxillary triangle, dissection should include also the submental triangle and the upper deep cervical triangle, anterior and posterior, on the right, down to the omohyoid muscle. If metastases are present in the right upper deep cervical triangle, the dissection should include at least the right submaxillary triangle and the entire deep cervical chain, anterior and posterior, including the supraclavicular space. For metastasis in the submental triangle, dissection should include the submental and both submaxillary triangles. It is also frequently advisable, as in this case, to expose partially the upper deep cervical lymphatics for inspection and palpation before definitely deciding on the limits of the operation.

Since the Tumor Service was organized at the Edward Hines Jr. Hospital in 1931, there have been 525 cases of true carcinoma of the lower lip treated (1931-1936) in addition to ninety keratoses or other precancerous lesions, or a total of 615 cases. In approximately 22 per cent of the cases of carcinoma of the lip cervical metastases were present or developed later. Many of these cases had been neglected and were advanced at the time of admission. Many had been previously and improperly treated. It is apparent that this incidence of metastasis is much higher than that when early and adequate treatment is given.

The accompanying tables show the results in the last thirty-three consecutive cases in which dissections of the neck were done during the past three years. All cases had a biopsy diagnosis, but all were not graded microscopically. It has been found difficult to grade some lesions accurately.

Cervical nerve block combined with local infiltration was the anesthesia used in most of the cases. In some, rectal ether supplemented with intratracheal anesthesia was employed. This also is very satisfactory. Avertin with amylene hydrate was abandoned after some untoward reaction in a few cases. There was no operative mortality in this series.

TABLE 3.—*Six Cases of Carcinoma (Squamous Cell, Keratinizing) of the Lip: Clinically the Glands Were Advanced, of Borderline Operability*

Case No.	Date	Name	Primary Lesion	Neck	Type of Operation	Glands Microscopically	Postoperative Irradiation	Result
1	1/21/35	F. P.	Advanced- grade 2-3	Right submaxillary, hard, 5 cm., 4 mo. fixed	Right suprahyoid	Positive	Yes	Well October 1937
2	4/25/35	D. L.	Entire lip 1 yr.; grade 2-3	Left submaxillary, hard, ulcerated, fixed	Left suprahyoid and seeds	Positive	Yes	Well October 1937
3	12/26/35	F. R.	Scar, only	Right submaxillary, hard, fixed, cm.	Right suprahyoid and seeds	Positive	Yes	Probable recurrence in February 1937; not heard from since
4	3/13/36	W. G.	Treated elsewhere	Right submaxillary, hard, fixed, 4 cm.	Right suprahyoid and seeds	Positive	Refused further treatment; metastasis left submaxillary in June 1936; had surgery and irradiation elsewhere; died April 1937, cervical metastatic cancer	
5	8/28/36	J. P.	Left 2 cm.; grade 2	Left submaxillary, hard, 3 cm., partly fixed	Left suprahyoid	Positive	Yes	Well October 1937
6	5/20/37	E. B.	Indurated scar midline, result of paste treatment	Fixed, hard, right submaxillary, 7 cm., partly fixed; hard left submaxillary, 6 cm., posterior cervical bilateral 1-2 cm. (several); posterior irradiation (elsewhere); probably inoperable	Complete bilateral dissection (2 stages)	Positive, bilateral	Yes	Recurrence October 1937

In these six cases, in which there were advanced cervical glands of borderline operability, the glands were microscopically positive in all six cases. Three patients are living and well. One has recurrent carcinoma in the neck; one probably had recurrent carcinoma in neck when last heard from in February 1937, and one died of recurrent carcinoma in the neck. The sixth patient, who now has recurrence, had been considered inoperable and a terminal case by a private radiologist and had been given irradiation to the neck. A cure was hardly expected by radical surgery but it was hoped at least to prolong his life.

Unilateral dissection of the upper part of the neck was done in five of these cases because of the patients' general poor condition. The opposite side of the neck was observed. Further treatment was not required in four of these six cases. In many cases of this type it is probably justified, and indicated, to do a dissection of the upper part of the neck on the opposite side two or three weeks after the first operation.

TABLE 4.—*Two Cases of Carcinoma (Squamous Cell, Keratinizing, of the Lip): Clinically Operable Glands, Treated by Simple Node Excision and Implantation of Radon Seeds*

Case No.	Date	Name	Primary Lesion	Neck	Preoperative Irradiation	Type of Operation	Glands Microscopically	Postoperative Irradiation	Result
1	6/29/34	W. G.	5.5 cm. 14 mos.; grade 2-3	Multiple hard glands, 1-2 cm.	Yes	Enlarged nodes excised and seeds	Positive	No	Died of metastatic carcinoma 9/20/35
2	11/22/34	P. D.	2 cm.; treated 6 mos. by caustics	Submental firm, 1 cm.; right submaxillary firm, 1 cm.	Yes	Enlarged nodes excised and seeds (12/28/34); recurrent nodes excised and seeds (2/12/35)	Positive	No	Died of metastatic carcinoma 12/9/35

In these two cases, in which there were clinically operable glands, the glands were microscopically positive. External irradiation was given, followed by excision of enlarged nodes and implantation of radon seeds. Both patients are dead of cervical metastases. This treatment is now not recommended for operable cervical metastases.

CONCLUSIONS

1. The results in thirty-one cases treated in the manner advocated are very gratifying. Twenty-eight of these patients are free from disease from a few months to more than three years.

2. Dissection of the neck is advocated when the primary lip lesion has been controlled and when there are enlarged cervical glands thought clinically to be metastatic.

3. Preoperative irradiation is not given. Postoperative irradiation, from 3,000 to 4,000 roentgens, is given in all cases in which the glands are microscopically positive for carcinoma.

4. Observation is advocated when enlarged cervical glands are thought to be inflammatory. Improving the condition of the mouth is all that is necessary in most of these cases.

5. When the cervical glands are not enlarged, neither irradiation nor neck dissection is advocated.

6. Neck dissection can be done as successfully after the glands are enlarged as before, provided operation is not deferred until the glands are large, fixed, ulcerated and inoperable.

7. Combined external and interstitial irradiation is employed in far advanced, palliative cases.

8. Probably no other tumor condition is treated in more ways, or regarding which opinion is more divided and treatment less standardized, than in metastatic carcinoma of the neck.

PULMONARY COMPLICATIONS

FOLLOWING 1,333 ADMINISTRATIONS OF CYCLOPROPANE

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During the past five years a new anesthetic gas, cyclopropane, has been gradually introduced into medicine. Its anesthetic properties were discovered in 1929,[1] and its true value has since been established step by step by active cooperation among anesthetists and surgeons,[2] physicians[3] and physiologists and pharmacologists,[4] particularly those at the University of Wisconsin.

The method of introduction, although the gas is revolutionary in its field, has been a model of cautious statement, completely lacking in the publicity and exploitation that has accompanied lesser events.

The new and unique value of cyclopropane lies in the high oxygen content with which it can be used. For instance, two patients at St. Luke's Hospital were anesthetized directly from an oxygen tent, were returned to the tent after operation and recovered.

Other features of this anesthetic, such as ease and pleasantness of induction,[5] greater relaxation than that produced by other gaseous anesthetics, quick elimination[6] and applicability for special surgical procedures, particularly thoracic operations,[7] have been stressed in numerous papers.

Along with these advantages, another, in the form of a definite reduction in the incidence of postoperative pulmonary complications following its use, is gradually being established. The figures that follow further substantiate this tendency.

This does not mean that the anesthetic is regarded as the sole cause of postoperative pneumonia. In fact, the pendulum has swung so far that now some authorities actually maintain, arguing from the fact that pulmonary complication follows as frequently after spinal anesthesia, that the anesthetic has nothing at all to do with this complication.

At St. Luke's Hospital we like to think that the anesthetic affects the results directly (1) through the degree of damage or excessive irritation produced in the respiratory tract and (2) through the degree of bodily depression produced by the anesthetic itself[8] (against that produced by the surgical measures) because of excessive relaxation and prolonged action. Whatever belief may be held regarding the cause of postoperative pulmonary complications, it is obvious that the irritated, mucus-laden respiratory tract is more likely to produce obstruction and atelectasis[9] than the unobstructed tract.

Judged merely from these two points, without recourse to statistical material, the advantage of cyclopropane over ether for depth of anesthesia sufficient for abdominal operation is obvious.

The direct effect of the anesthetic has been increasingly overshadowed in recent years by other factors, which, in the aggregate, probably do have a more important influence on results than the anesthetic itself. The factors concerned in the production of postoperative pulmonary complications are (1) the anesthetic agent, including the technic of administration and recovery, (2) the site of the operative procedure, (3) the duration of the operation, (4) sex, (5) the preoperative condition of the patient, including age, and (6) the depth of anesthesia. Contemplation of this list shows how broad the problem is, involving many aspects of anesthesia and surgery.

The way selected to present my statistical material on cyclopropane has been to correlate the observations with these six factors. This is the reverse of the usual procedure, which is to study the statistics and emerge with the conclusion that the foregoing six factors are important in the production of postoperative pulmonary complications. What is attempted here is to correlate the specific properties of this anesthetic, through the factors mentioned, to the problem under consideration.

THE AGENT

In the twenty-five month period ended Aug. 1, 1937, cyclopropane anesthetic had been administered 1,333 times in my own practice, in cases which were subsequently observed and studied. Thirteen complications developed, to make an incidence of 0.97 per cent.

1. Lucas, G. H. W., and Henderson, V. E.: A New Anesthetic Gas: Cyclopropane, Canad. M. A. J. **21**: 173 (Aug.) 1929.

2. Waters, R. M., and Schmidt, E. R.: Cyclopropane Anesthesia, J. A. M. A. **103**: 975 (Sept. 29) 1934.

3. Kurtz, C. M.; Bennett, J. H., and Shapiro, H. H.: Electrocardiographic Studies During Surgical Anesthesia, J. A. M. A. **106**: 434 (Feb. 8) 1936.

4. Seevers, M. H.; Meek, W. J.; Rovenstine, E. A., and Stiles, J. A.: A Study of Cyclopropane with Especial Reference to Gas Concentrations, Respiratory and Electrocardiographic Changes, J. Pharmacol. & Exper. Therap. **51**: 1 (May) 1934.

5. Neff, W. B., and Stiles, J. A.: Some Experiences with Cyclopropane Anesthetic, with Special Reference to the Diabetic Patient, Canad. M. A. J. **35**: 56 (July) 1936.

6. Seevers, M. H.; De Fazio, S. F., and Evans, S. M.: A Comparative Study of Cyclopropane and Ethylene with Reference to Body Saturation and Desaturation, J. Pharmacol. & Exper. Therap. **53**: 90 (Jan.) 1935.

7. Rovenstine, E. A.: Cyclopropane Anesthesia in Thoracic Surgery, Anesth. & Analg. **14**: 270 (Nov.-Dec.) 1935. Eversole, U. H., and Overholt, R. H.: Anesthesia in Thoracic Surgery with Special Reference to Cyclopropane, J. Thoracic Surg. **5**: 510 (June) 1936.

8. Henderson, Yandell: Atelectasis, Massive Collapse and Related Postoperative Conditions, Bull. New York Acad. Med. **11**: 639 (Nov.) 1935.

9. Coryllos, P. N.: Postoperative Pulmonary Complications and Bronchial Obstruction, Surg., Gynec. & Obst. **50**: 795 (May) 1930.

Waters, Bennett and Taylor [10] reported an incidence of 0.95 per cent after 5,889 administrations.

Several reports on postoperative complications following cyclopropane anesthesia have been gathered and are summarized in table 1. The results are compared to those following the use of older anesthetics, chiefly nitrous oxide-ether. The comparison, with an occasional exception, is favorable to cyclopropane.

This statistical table is considered important to this paper and warrants further comment about postoperative complication statistics in general.

One observation often made is that the more exacting a study becomes the higher the incidence is found to be. For instance, King [11] found at the Massachusetts General Hospital in the first year of his extensive studies that, amazingly enough, only 44 per cent of the pulmonary complications actually present found their way to the discharge sheet (from which most permanent hospital records are compiled). His over-all incidence after correction ranged from 3.7 per cent in 1929 to 6.8 per cent in 1931. Against these figures, in another report from a nearby hospital the incidence was found to be only 0.56 per cent. The difference for abdominal operations alone in these two reports was even greater. Possibly the later figures were made from the record room figures alone.

Whipple [12] reported somewhat the same experience as did King. At the Presbyterian Hospital in 1914 and 1915, when no special study of pulmonary complications was in progress, forty-one cases were uncovered. In the following two years, during a special study, ninety-one cases were found. His over-all incidence was found to be 2.6 per cent. One year later, the special study being continued, it was 3.3 per cent (Cleveland). Eliason and McLaughlin [13] stated that each succeeding year the study is carried on in a given institution the higher the figures become, and Cleveland [14] showed that as the figures become higher in each succeeding year the incidence of obscure postoperative "reactions" diminishes.

Therefore, with occasional exceptions, the incidence after ether is so much higher than after cyclopropane that it raises the question of the accuracy of record keeping in the cases in which cyclopropane is used. This criticism, however, does not hold. The chief source of mass statistics on cyclopropane is the University of Wisconsin. The methods of record keeping there have been explained in detail [15] and are unsurpassed anywhere. The other data given in table 1 were compiled from a small number of cases, with the resulting likelihood of minimizing error. Furthermore, if the report from this institution possesses any merit, one reason should be that the idea of reporting the results of pulmonary complications was considered even before the first administration of the new anesthetic was performed, and subsequent observations were made with that intention in view. Personal records and observations have here also increased the number of complications uncovered over those reported on the discharge sheet.

Ether was required to fortify the action of cyclopropane in many cases, particularly during the early months. The decrease in the amount of ether used has been steady. The increase in pulmonary morbidity resulting from the addition of ether is shown in table 2.

As surgeons become more familiar with operating with the patient under cyclopropane anesthesia less ether is requested. One great advantage (from the basis of pulmonary morbidity) of cyclopropane is that when it is used muscles do not completely lose their tone. Respirations are so quiet, however, that "pushing" in the abdominal field causes little trouble except at the beginning, before pads are placed. Unfortunately, any trouble at the beginning usually causes the surgeon

TABLE 1.—*Comparison of Cyclopropane and Ether*

Reference	Ether				Cyclopropane			
	Total Cases	Complications, Percentage	Abdominal Operations	Complications, Percentage	Total Cases	Complications, Percentage	Abdominal Operations	Complications, Percentage
This series	.....	....	.....	....	1,333	0.97	626	2.07
Waters, Taylor and Bennett [10]	2,431	1.82	.....	....	5,889	0.95		
Bogan, J. B.: Anesth. & Analg. **15**: 275 (Nov.-Dec.) 1936	.....	....	.....	....	315	0	172*	0
Moffitt, J. A., and Mechling, G. S.: Anesth. & Analg. **15**: 225 (Sept.-Oct.) 1936	.....	....	.....	....	300	0.67	109	1.8
Griffith, H. R.: Anesth. and Analg. **14**: 253 (Nov.-Dec.) 1935	.....	....	.....	....	1,108	0.0†		
Wiggin, S. C.: Anesth. & Analg. **15**: 105 (May-June) 1936	1,593	0.56	670*	1.04*				
Ryan, T. J.: Hyperventilation in Abdominal Surgery, J. A. M. A. **107**: 267 (July 25) 1936	.....	....	411	1.70				
King [11]	.....	3.70‡ 5.20 6.80	1,012‡ 1,198	12.2‡ 13.1				
Gray [19]	.....	....	276§ 3,153	4.3 6.2¶				
Watter, Leonid: Anesth. & Analg. **15**: 22 (Jan.-Feb.) 1936	.....	....	1,455	7.0‖				
Fuller, C. J.: Lancet **1**: 115 (Jan. 18) 1930	1,478	8.30						
Eliason and McLaughlin [13]	7,326	1.68						
Cleveland [14]	1,940	3.30						
Whipple [12]	3,719	2.60						

* Approximate.
† Definite postoperative pneumonia.
‡ Different years.
§ Trendelenburg position, postoperative.
¶ Normal position, postoperative.
‖ Mostly abdominal operations.

10. Taylor, I. B.; Bennett, J. H., and Waters, R. M.: Anesthesia at the Wisconsin General Hospital: Anesthetic Methods and Postoperative Respiratory Complications, Anesth. & Analg. **16**: 198 (July-Aug.) 1937.
11. King, D. S.: Postoperative Pulmonary Complication: A Statistical Study Based on Two Years' Personal Observation, Surg., Gynec. & Obst. **56**: 43 (Jan.) 1933.
12. Whipple, A. O.: A Study in Postoperative Pneumonitis, Surg., Gynec. & Obst. **26**: 29 (Jan.) 1918.
13. Eliason, E. L., and McLaughlin, Charles: Postoperative Pulmonary Complications, Surg., Gynec. & Obst. **55**: 716 (Dec.) 1932.
14. Cleveland, M.: Further Studies in Postoperative Pneumonitis, Surg., Gynec. & Obst. **28**: 282 (March) 1919.
15. Rovenstine, E. A.: A Method of Combining Anesthetic and Surgical Records for Statistical Purposes, Anesth. & Analg. **13**: 122 (May-June) 1934. Rovenstine, E. A., and Taylor, I. B.: Postoperative Respiratory Complications: Occurrence Following 7,874 Administrations, Am. J. M. Sc. **191**: 807 (June) 1936.

to request ether immediately. Forbearance for the first two or three minutes will usually allow considerable diminution in the amount or, frequently, the entire elimination of ether. The advantage of this lies in the quicker elimination of the anesthetic (hypoventilation consideration) and the reduction of irritation in the respiratory tract (obstruction consideration).

The technic of administration has been chiefly that of continuous flow,[16] with absorption of carbon dioxide. Waters in numerous papers has established the value of the absorber.[17] The advantages of a controlled and conditioned atmosphere with minimal heat loss and shock has a distinct bearing on pulmonary complication.

The continuous flow method of administration affects results only through preserving a higher percentage of inert gas (nitrogen) in the respired mixture by the use of a partially distended bag instead of a full one. Recently the routine technic of administration used at St. Luke's has involved the regular addition of inert gas, chiefly helium, to the anesthetic mixture. This problem, the relationship of nitrogen and other inert gases to pulmonary complications, has been extensively discussed elsewhere by Jones and me.[18]

Features of the recovery period emphasized include the immediate placing of the patient on his side on the stretcher and in bed. The matter of position has been stressed recently at the Mayo Clinic[19] among other places, where the Trendelenburg position has been used postoperatively to increase drainage of the pulmonary tract as well as to expedite venous return from the legs. Here at St. Luke's the side position is preferred as a better one for drainage, freedom for coughing and vomiting. Venous return from the legs is aided by the necessary motion required of the patient (actively and passively) in getting into and out of the position. The exact position has recently been described by Dill.[20] We have used it for eight years and copied it in the beginning from an anesthetist who had already used it many years.

Emphasis is also placed on the anesthetist accompanying the unconscious patient on the return to his room. One life, beyond any reasonable doubt, has been saved by this routine procedure.

Carbon dioxide by direct addition is not used. A mild hyperpnea during the latter part of the operation, utilizing the patient's own carbon dioxide by means of an open end extension to the respiratory tract, is usually produced.

TABLE 2.—*Postoperative Morbidity Following Cyclopropane Anesthesia With and Without Ether as a Supplement (From January 1936 to July 1937, Inclusive)*

Classification	Cases	Complications	Percentage
All abdominal operations	517	11	2.12
Abdominal operations—ether supplement	303	9	2.97
Abdominal operations—no supplement	214	2	0.93

Note: No ether was used when the operation was not abdominal except in five cases of hemorrrhoidectomy, in which it was given for the purpose of prolonging the relaxation of the sphincter muscle, and in one other case under special circumstances.

16. Burford, G. E.: Continuous Flow Administration of Cyclopropane, Anesth. & Analg. **15**: 254 (Sept.-Oct.) 1936.
17. Waters, R. M.: Carbon Dioxide Absorption from Anesthetic Atmospheres, Proc. Roy. Soc. Med. **30**: 1 (Jan.) 1936.
18. Jones, O. R., and Burford, G. E.: Massive Atelectasis Following Cyclopropane Anesthesia: Report of Cases and a Theory of Cause and Prevention, this issue, p. 1092.
19. Gray, H. K.: Postoperative Pulmonary Complications and the Postoperative Use of the Trendelenburg Position, Minnesota Med. **18**: 273 (May) 1935.
20. Dill, W. W.: Postoperative Position, Anesth. & Analg. **16**: 70 (Jan.-Feb., supp. pages) 1937.

THE SITE OF OPERATIVE PROCEDURE

In this series 626 of the 1,333 operations either were abdominal or otherwise involved the peritoneum (operations for inguinal and femoral hernias and kidney operations). The entire thirteen complications developed in these cases.

There was no complication in 707 cases of extra-abdominal operation. In our experience the problem of pulmonary complication following inhalation anesthesia for operations not on the abdomen has always been negligible. However, we do a minimal number of intracranial operations, which are considered to carry a high pulmonary morbidity.[10]

TABLE 3.—*Comparison Between Individual Operations Done with Cyclopropane and Those Done with Other Anesthetics*

	Cases	Pulmonary Complications: Number	Pulmonary Complications: Percentage	Mortality, Percentage of Morbidity
Stomach (present series, cyclopropane)	23	5	21.7	40.0
Stomach (ward series, no cyclopropane)	291	26	8.9	50.0
Gallbladder and ducts (cyclopropane)	88	3	3.4	0
Gallbladder and ducts (ward series, no cyclopropane)	485	20	4.1	15.0
Inguinal hernia (cyclopropane)	61	0	0	0
Inguinal hernia (ward series, no cyclopropane)	927	34	3.6	5.8

The main factor to which is attributed the high incidence of pulmonary complications following abdominal operations is the decreased ventilation and vital capacity of the lungs[21] subsequent to opening the peritoneum, together with the voluntary restriction of respirations because of pain subsequent to peritoneal irritation. In this regard the value of the technic of administration now used at St. Luke's Hospital,[18] requiring the addition of inert gas to the anesthetic mixture and thus prolonging the absorption time of the gases in the hypoventilated or even completely static portions of the lung, is evident.

The other important point associated with the abdominal site of operation as a producer of postoperative complications is the increased depth of anesthesia that necessarily accompanies operations in this area. This will be discussed under depth of anesthesia.

For different types of abdominal operations the incidence of complications varies interestingly. Data on this phase, together with comparisons of results for specific operations from wards where cyclopropane is not used, are given in table 3. The facts are discussed later.

DURATION OF OPERATION

The extreme importance of the duration of the operation has received insufficient attention. All persons concerned with the problem of postoperative pulmonary complications might well become familiar with the figures of Waters, Bennett and Taylor[10] (table 10 of their paper). These, based on 12,349 cases, show the incidence to increase from 2.9 per cent (all complications, major and minor) for an operation of one-half hour, through decided successive stages for each half hour the operation is prolonged, to 30 per cent for operations lasting from three hours to three and one-half hours. These figures

21. Churchill, E. D., and McNeil, Donald: The Reduction in Vital Capacity Following Operation, Surg., Gynec. & Obst. **44**: 483 (April, pt. 1) 1927. Muller, G. P.; Overholt, R. H., and Pendergrass, E. P.: Postoperative Pulmonary Hypoventilation, Arch. Surg. **19**: 1322 (Dec., pt. 2) 1929.

show a continuation of the tendency established a year earlier, reported by Rovenstine and Taylor.[15] Their figures showed the incidence for operations lasting one and one-half hours to be double that for operations lasting one hour. At two hours the incidence tripled that at one hour.

Evidently the pendulum has swung too far to the other side, away from the incision of "an inch and a half in a minute and a half."

In the present series, the average duration of anesthesia in the thirteen cases in which complications developed was one hour and thirty-eight minutes. In only one of the thirteen cases did complications develop after an operation lasting less than one hour. This fact was outstanding. Together with the high incidence of complications following prolonged operations on the stomach, reported in table 3, it caused us to inquire whether the incidence of morbidity is not unduly increased with cyclopropane anesthesia in operations of a prolonged nature, at least over the otherwise very low incidence for this anesthetic. The average duration of anesthesia in the five cases in which complications developed after operations on the stomach was two hours and one minute, while morbidity for the entire group of operations on the stomach was 21.7 per cent.

SEX

Mark Twain might better have said of sex, at least in relation to anesthesia, what he said of the weather, that "everybody talks about it but nobody does anything about it." A suggestion is here advanced for doing something about it.

Eliason and McLaughlin,[13] King,[11] Brock[22] and others have written of the greater incidence of complications for males than for females. Eliason and McLaughlin showed that 70 per cent of their cases occurred in males. King found complications twice as frequently in males. Brock reported sixty-two of eighty-five cases in males.

It is unquestioned that males show a greater predisposition to pulmonary complications after anesthesia. The approximate figure is more than two to one. King went further to say that sex, with the site of operation, is the most important predisposing factor to postoperative pulmonary complications.

It is also unquestioned that the administration of anesthetics to males is more difficult than to females. Difficulty of induction has been shown by Guedel[23] to result largely from an elevation of the metabolic rate. The metabolic rate represents the degree of reflex irritability and oxygen want. It represents a fair approximation of the depth of anesthesia that must be traversed before the stable planes of third stage anesthesia (Guedel classification) are reached. The difficulty of induction disappears as the metabolic rate is brought down. The greater the depth to be traversed the greater is the likelihood of an uneven, struggling induction.

In the first place, metabolism in male tissue is the more active, producing on the average 40 calories per square meter body surface per hour, to 37 calories for female tissue. Furthermore, muscular action, once initiated, is much more intense in males. This results in subsequent derangement in the anesthetic atmosphere through losses and subsequent additions of the anesthetic, usually, influenced by the behavior of the patient, in too high concentration. This in turn leads to an uneven, irregular induction, a process which, in its optimal form, should be a smooth progression both of succeeding stages in the depth of anesthesia and of increasing concentrations of the anesthetic in the respired atmosphere.

In practice the difficulty of induction of a premedicated male is about equal to that accompanying the induction of an unpremedicated female. A heavily (properly) premedicated male is looked on as no more difficult than the average female. The unpremedicated male there is no excuse for.

What I propose to do about sex then is to (1) increase the preliminary medication of males enough to bring them to the operating room almost asleep, with metabolic rates greatly depressed, and as nearly as possible insusceptible to the stimuli of their surroundings, the medication being given far enough ahead (for instance, one and one-half hours for morphine) to have reached its maximum effect before the anesthesia is started and to be wearing off as the anesthesia progresses, and (2) to use cyclopropane, the rapid induction of which, when desired, takes effect with a minimal amount of stimulation, muscular activity and subsequent metabolic elevation.

This may be a too didactic treatment of the controversial subject of heavy preliminary medication, the argument against which I have chosen to avoid.

In this series seven males and six females had pulmonary complications. The total number of females operated on was greater than that of males, but the incidence of complications in males was still nothing like 2 to 1. Nor has universal acceptance of heavy preliminary medication for males as yet been achieved.

PREOPERATIVE CONDITION OF THE PATIENT

It has long been observed that elderly, debilitated, septic or acutely ill patients are more prone to postoperative complications. Waters, Bennett and Taylor[10] have recently given statistical evidence on this point. They showed that a preoperative estimate of the patient as a risk checked closely with the postoperative development of complications.

In this series, however, no marked confirmation of these facts was obtained. No routine preoperative estimate of all patients was made. Five of the thirteen patients who had complications were found to be good risks, and only two exceeded 50 years of age. These observations call further attention to the possibility that pulmonary complications after cyclopropane anesthesia depend on other factors, such as physical differences in the anesthesia atmosphere,[18] rather than on the routine ones so clearly established for other anesthetics.

DEPTH OF ANESTHESIA

On the important subject depth of anesthesia, surgeons and anesthetists sometimes disagree.

The only statistical information available (again from Waters, Bennett and Taylor[10]) shows complete confirmation of the long held belief that pulmonary complications increase as the depth of the anesthesia increases.

The value of relaxed abdominal muscles and quiet respirations is obvious to all concerned. It should be more generally appreciated, however, that increase of the former through deeper anesthesia does not produce the latter. Increased depth produces intercostal paralysis and marked diaphragmatic excursions, with

22. Brock, R. C.: Postoperative Chest Complications: A Clinical Study, Guy's Hosp. Rep. **86**: 191 (Jan.-April) 1936.
23. Guedel, A. E.: Anesthesia, A Teaching Outline: Preparation of the Patient and Mechanism of Varying Anesthesia Requirements, Anesth. & Analg. **15**: 157 (July-Aug.) 1936.

resulting increased motion of the abdominal contents. This problem lately has been approached from another angle, with some success.[24] Apneic periods are deliberately produced and maintained by artificial respirations, with marked reduction in abdominal motion.

The implications of deep anesthesia are broad and should be generally understood and carefully weighed. Guedel[25] stated that relaxed vascular (smooth muscle) tone accompanies marked loss of skeletal muscle tone from anesthesia paralysis. This results in impaired circulation and a tendency to shock. He estimated that to carry a patient fifteen minutes in lower third plane anesthesia is more depressing than to carry him two hours in the first plane.

Henderson[8] called attention to the loss of tonus, with resulting venous stasis and diminished return of blood to the heart, that accompanies deep anesthesia. Actual measurements of intramuscular pressure, which is concerned with venous return, have been recorded.[26] The readings showed a decrease from 73 mm. (average) of water before operation to 48 mm. (average) after anesthesia and operation. It can readily be seen that this and the preceding factor together form a vicious circle and hasten shock. Henderson[8] further stated: "The respiratory center exerts at times a dominating control not only over respiratory muscles but over the entire musculature. Profound anesthesia may stop respirations and abolish tonus. The demand of the surgeon for extreme relaxation increases the tendency to serious postoperative sequelae."

With regard to depth of anesthesia, the contrast between the incidence of pulmonary complications developing after abdominal operations and after nonabdominal operations in this series is interesting: 626 abdominal operations, 2.07 per cent, and 707 nonabdominal operations, none.

One outstanding difference (among others not directly related) in the conditions surrounding these two groups is the increased depth of anesthesia necessary for abdominal work. In this series at least eleven of the thirteen patients with complications were brought to deep third stage anesthesia during the course of the operation.

Until recently the value of an anesthetist was determined by his ability to produce and maintain deep anesthesia. Considerably more thought is now being given to this factor and its relationship to the expansive problem of postoperative pulmonary complications, as outlined here, especially in the light of results following cyclopropane anesthesia. The great advantage of cyclopropane is that it produces a certain degree of muscular relaxation which only rarely can be exceeded. This property has in some instances initiated a tolerance for incomplete relaxation where it did not exist previously. If this tendency receives further impetus it will have the backing of the sound arguments of physiology.

TABLE 4.—*Summary of Thirteen Cases in Which Complications Developed*

Diagnosis	Age	Sex	Pulmonary Complication	Day of Onset	Minutes of Anesthesia	Result and Miscellaneous Information
Appendectomy; acute appendicitis.....	26	F	Atelectasis (slight)	Day of operation	65	Lungs clear forty-eight hours; cured
Polya's resection of stomach.....	40	M	Atelectasis (severe)	Day of operation	145	Lungs clear forty-eight hours; cured
Cholecystectomy; exploration of common duct	48	M	Embolic pneumonia	13	75	Cured; sudden onset with hemoptysis
Second operation fifth day after spinal anesthesia for Polya's resection of stomach; intestinal obstruction; freeing adhesions of stomach	45	F	Embolic pneumonia	16	75	Cured; patient out of bed at onset of pulmonary symptoms
Appendectomy; acute appendicitis.....	43	M	Broncho-pneumonia	1	82	Cured; acute pharyngitis and chest rales preoperatively
Resection of stomach.....	50	M	Broncho-pneumonia or atelectasis	3	170	Improved; long stormy postoperative course with indefinite chest signs and x-ray appearances
Appendectomy; acute appendicitis.....	39	M	Broncho-pneumonia	8	78	Cured
Hysterectomy; appendectomy	45	F	Broncho-pneumonia	1	135	Cured; long difficult hysterectomy, plus injury to bladder
Cholecystectomy	55	F	Pneumonia	5	95	Cured; postoperative course marked by phlebitis and infection of wound
Hysterectomy; salpingo-oophorectomy ...	36	F	Pneumonia	6	90	Cured; phlebitis developed on the fourteenth postoperative day; second "pneumonia," right apex, eighteenth postoperative day
Polya's resection of stomach; bleeding ulcer	46	M	Pneumonia	3	96	Died ninth postoperative day; hemoglobin from 32 to 45 per cent
Resection of stomach; bleeding ulcer.....	38	M	Pneumonia?	2	120	Died seventh postoperative day; diagnosis of pneumonia not established; no x-ray examination; continuous vomiting
Cholecystectomy	60	F	Atelectasis	1	45	Lungs clear in three days; good recovery

ADDITIONAL FACTORS

A few matters not included under the preceding six headings remain to be discussed.

Table 4 shows a summary of the facts on which this study is based. The column "Miscellaneous Information" shows that possibly one or two of the cases might have been omitted. On the other hand, another case, in which the complication was undiagnosed for many months after its occurrence and ran its entire course of alarming symptoms in the operating room within twenty-five minutes of the operation, the patient showing no pulmonary morbidity on return to his room, was not included. This case has been reported elsewhere.[18] Two cases of sudden death (sixth and eighth postoperative days) were treated as vascular accidents. A case of mediastinitis subsequent to a traumatic accident accompanying endotracheal intubation with the patient under tribromethanol-cyclopropane-ether anesthesia was not included.

An interesting observation in connection with this table is the low mortality in relation to postoperative

24. Guedel, A. E., and Treweek, D. N.: Ether Apneas, Anesth. & Analg. **13**: 263 (Nov.-Dec.) 1934. Burford, G. E.: Utilization of Anesthesia Apneas, Anesth. & Analg. **16**: 108 (March-April) 1937. Waters.[17]

25. Guedel, A. E.: Anesthesia, A Teaching Outline: Anesthetic Depths, Surgical Reflexes, Stages and Operations, Anesth. & Analg. **15**: 120 (May-June) 1936.

26. Henderson, Yandell; Oughterson, A. W.; Greenberg, L. A., and Searle, C. P.: Muscle Tonus, Intramuscular Pressure and the Venopressor Mechanism, Am. J. Physiol. **114**: 261 (Jan.) 1936.

pulmonary morbidity. Only two of the thirteen patients died, the mortality thus being 15.4 per cent of the morbidity. Other figures run from 20.3 (King, lowest year) to 32.5 (Eliason) and 33.3 (King, highest year) per cent.

Data on the postoperative deaths occurring in this series during the first twenty-three months is given in table 5. No death was attributed to the anesthesia. One death occurred on the table because of shock and massive hemorrhage.

The Council on Pharmacy and Chemistry of the American Medical Association gave great weight to information on deaths in its report [27] on cyclopropane, withholding official recommendation chiefly because a series of 2,200 cases of Waters and Schmidt showed a mortality rate of 4.19 per cent compared to a rate of 3.99 per cent for other inhalation anesthetics.[28] To others this information might seem less important, since a high mortality figure results, among other things, from such uncontrollable factors as the number of patients with inoperable or borderline carcinoma who are encountered and the number of days an appendix has been inflamed before the patient comes to operation.

In another paper Jones and I [18] showed the slight but definite possibility of a sudden respiratory death following administration of cyclopropane (because of massive collapse of an entire lung). Three cases with autopsy gathered from various sources were reported. This rare occurrence should be considered in any discussion of the pulmonary complications following cyclopropane anesthesia.

TABLE 5.—*Data on Deaths Following the Administration of Cyclopropane*

Cases (23 months)	1,206
Total deaths	35
Mortality	2.90%
Time of death	
Day of operation	1
Day after operation	
1	2
2-3	3
4-7	11
2d week	4
Later	14
Cause of death	
Pneumonia	2
Embolism	2
Hemorrhage	1
Infection	11
Uremia	1
Carcinoma	16
Others	2

SUMMARY

In an attempt to correlate the statistical material resulting from a study of 1,333 administrations of cyclopropane to the problem of postoperative pulmonary morbidity, the latter was shown to be a broad one involving many factors in anesthesia and in surgery. Over some of these factors more control may exist than is at present being generally utilized.

The outstanding observation is the relatively low figure both for the incidence of pulmonary morbidity and for the morbidity-mortality ratio following cyclopropane anesthesia. This continues the trend established by others in previous reports.

395 Riverside Drive.

27. Cyclopropane for Anesthesia, Report of the Council on Pharmacy and Chemistry, J. A. M. A. **106**: 292 (Jan. 25) 1936.

28. Schmidt, E. R., and Waters, R. M.: Cyclopropane Anesthesia: Postoperative Morbidity in 2,200 Cases, Anesth. & Analg. **14**: 1 (Jan.-Feb.) 1935.

MASSIVE ATELECTASIS FOLLOWING CYCLOPROPANE ANESTHESIA

REPORT OF CASES AND A THEORY OF CAUSE AND PREVENTION

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During the past two years, four deaths following quickly after the administration of cyclopropane have come to our attention. Autopsy, when performed, showed massive atelectasis of one or both lungs. Furthermore, pulmonary complications following long-continued cyclopropane anesthesia, especially for operation on the stomach,[1] have increased more than should be expected over the otherwise low incidence of such complications following the administration of cyclopropane.[2]

These facts we regard as sufficient reason for a critical examination of the physical conditions involved in the administration of cyclopropane. The relationship of these conditions to the development of massive atelectasis and the greater likelihood of subsequent development of partial atelectasis are considered in detail.

In a paper of this nature we feel it necessary to state unequivocally our position on cyclopropane anesthesia.

The manner of the introduction of this drug has been a model of careful statement and restraint. Even though completely revolutionary in its field, the discovery of the anesthetic properties of cyclopropane by Henderson and Lucus and the subsequent work of Waters and his associates progressed quietly, without any of the publicity and exploitation that have accompanied many lesser events.

No one can witness the successful anesthetization of, operation on and subsequent recovery of patients taken directly from oxygen tents without realizing the unique value of cyclopropane anesthesia. Theirs are extreme cases to be sure, and far more valuable in the aggregate is the comfort of the large number of patients who receive the benefit of a quiet and pleasant induction. The complete disappearance of anoxemia with this anesthesia has prevented many of the bodily derangements due to the lack of oxygen. The ephemeral action of this gas and its ability to produce anesthesia deep enough for laparotomy are qualities which add to its importance.

With full knowledge of the value of cyclopropane, we propose in this paper a suggestion both for avoiding the rare tragedy of massive atelectasis and for reducing the already low figures for postoperative morbidity associated with this type of anesthesia.

The circumstance producing complete atelectasis of a whole lobe has of recent years been assumed to be obstruction in the main bronchus followed by absorption of the alveolar gases behind the obstruction. When the obstruction has become effective, the time required

From the Department of Anesthesia and the Medical Service of St. Luke's Hospital.

1. Burford, G. E.: Pulmonary Complications Following 1,333 Administrations of Cyclopropane, this issue, p. 1087.

2. Taylor, I. B.; Bennett, J. H., and Waters, R. M.: Anesthesia at the Wisconsin General Hospital: I. Anesthetic Methods and Postoperative Respiratory Complications, Anesth. & Analg. **16**: 187 (July-Aug.) 1937. Griffith, H. R.: Cyclopropane Anesthesia, ibid. **14**: 253 (Nov.-Dec.) 1935. Bogan, J. B.: A Clinical Evaluation of Cyclopropane: After Its Use in 300 Surgical Anesthesias, ibid. **15**: 275 (Nov.-Dec.) 1936. Moffitt, L. A., and Mechling, G. S.: A Comparison of Cyclopropane with Other Anesthetics, ibid. **15**: 225 (Sept.-Oct.) 1936.

for the development of atelectasis depends on the rate of absorption by the lung of the gases distal to the obstruction, provided the circulation in the lung is intact and the alveolar epithelium undamaged.

Coryllos and Birnbaum [3] have shown the great variation that exists in the rate of this absorption. The anesthetic gases tested were absorbed in a matter of minutes, as were oxygen and carbon dioxide. The inert gases nitrogen, hydrogen and helium required from eighteen to twenty-six hours for absorption, which even then for helium was not complete.

When one keeps these facts in mind, consideration of the physical conditions surrounding the administration of cyclopropane shows that, with occasional minor failures in technic, the development of massive atelectasis during the actual administration, with or without the presence of the bronchial plug considered so typical of this condition, is at least a possibility.

To develop this idea further, it is plain that, when the mask is placed on the patient's face at the start of cyclopropane anesthesia, the character of the atmosphere being breathed is at first little changed. As the bag fills with cyclopropane and oxygen the resulting mixture changes its physical characteristics in that now a considerably greater proportion of the atmosphere consists of the rapidly absorbable gases that have been added. Nitrogen now comprises considerably less than the normal 79 per cent of the atmosphere.

But during the course of an operation, as a result of various maneuvers, the content of the bag may be partly lost two or three times. Each loss represents a further dilution of the inert gas (nitrogen) content of the bag both by direct loss of nitrogen and by reduction of the remaining percentage through refilling with quickly absorbable oxygen and cyclopropane. Thus with unsatisfactory technic, or as the result of unavoidable losses through other means, the anesthesia atmosphere after a considerable time may be devoid of inert gas except for the small amount of nitrogen brought from the tissues to the lungs by the blood in simple solution and diffused into alveoli. As the blood normally contains about 1 per cent nitrogen, this amount after two hours would probably be very small and its effectiveness in the alveoli accustomed to a nitrogen tension of 80 per cent would be negligible.

The significance of this fact is considerable. Rovenstine and Lemmer [4] have shown that the time required for a comparable degree of absorption of 600 cc. of gas by the lungs of dogs varies as follows: anesthetic and other gases—carbon dioxide one minute six seconds, oxygen one minute twenty-two seconds, nitrogen monoxide one minute forty-two seconds and ethylene two minutes two seconds; inert gases—nitrogen twelve minutes six seconds, hydrogen sixteen minutes twenty-two seconds and helium eighteen minutes six seconds.

Thus they emphasized, as did Coryllos and Birnbaum, the great rapidity of absorption of the anesthetic and active gases as compared with the inert "filler" gases. They observed under direct vision, after blocking the bronchus, that a specific degree of atelectasis appeared after the varying intervals stated for the different gases.

Toward the end of an operation the patient may be breathing an atmosphere made up almost entirely of rapidly absorbable gases, the inert gases having been lost during the anesthesia. When the alveoli of the lungs have lost the supporting properties of the inert gas nitrogen, conditions are present which favor atelectasis.

During an operation the patient's respirations are very quiet because of the preliminary opiates, the cyclopropane and the high oxygen content in the lungs. Together with these factors, which tend to set the stage for a possible collapse of the lung, there is the definite loss of body tonus resulting from the operation itself.[5] With long-continued shallow respirations, certain parts of the lungs, especially at the periphery, may not be ventilated at all. If, during the period of lack of ventilation, the gases in the resting alveoli consist of only rapidly absorbable oxygen and cyclopropane, it is possible that they may be completely absorbed before further ventilation takes place. Patches of atelectasis may thus develop without an obstruction in any portion of the bronchial tree.

This process, which may be termed creeping atelectasis, could go on, masked by the high oxygen content of the anesthesia atmosphere, until an entire lobe was involved. The first indication of it, beyond possibly an excessive amount of oozing in the operative wound, would appear when the mask was removed at the end of the operation. Then the lack of sufficient working surface of the lung, together with the lowered oxygen content of the inspired air and the increased demands of the body for oxygen on awakening, would soon make itself felt. The patient would show all of the symptoms of respiratory embarrassment, such as marked cyanosis, restlessness and, in some instances, cessation of breathing. The pulse would continue for a time even though the right side of the heart had the added burden of forcing blood through the partially or totally collapsed lungs.

Corylos and Birnbaum,[6] in a discussion of this matter in 1932 (before the general introduction of cyclopropane), expressed the opinion that the presence of nitrogen in the air is a fortunate circumstance of nature and that without it general anesthesia would be impossible because of the ease and rapidity of the formation of atelectasis. This was discussed in a theoretical vein. But even then, and for years previous to that time, before the widespread acceptance of the soda lime carbon dioxide absorber [7] that accompanied the introduction of cyclopropane to medicine, probably the majority of anesthetics were given in an atmosphere seriously lacking in nitrogen. In the now obsolete method of administering gas or gas and ether, a rapid flow of the agent was run through the mask and out into the air in order to carry away the accumulating carbon dioxide. The nitrogen was of course washed out with the carbon dioxide.

Thus physical conditions propitious for immediate development of massive atelectasis without bronchial obstruction in a patient under anesthesia on the operating table have existed for years. Yet to our knowledge only the two cases reported by Bergamini and Shepard [8]

3. Coryllos, Pol N., and Birnbaum, G. L.: Studies in Pulmonary Gas Absorption in Bronchial Obstruction: II. The Behavior and Absorption Times of Oxygen, Carbon Dioxide, Nitrogen, Helium, Hydrogen Ethylene Nitrous Oxide, Ethyl Chloride and Ether in the Lung, Am. J. M. Sc. **183**: 327 (March) 1932.

4. Lemmer, K. E., and Rovenstine, E. A.: Rate of Absorption of Alveolar Gases in Relation to Hyperventilation, Arch. Surg. **30**: 625 (April) 1935.

5. Henderson, Yandell: Atelectasis, Massive Collapse and Related Post-Operative Conditions, Bull. New York Acad. Med. **11**: 639 (Nov.) 1935.

6. Coryllos, Pol N., and Birnbaum, G. L.: Studies in Pulmonary Gas Absorption: III. A Theory of Air Absorption in Atelectasis, Am. J. M.Sc. **183**: 347 (March) 1932.

7. Waters, R. M.: Carbon Dioxide Absorption from Anesthetic Atmospheres, Proc. Roy. Soc. Med. **30**: 11 (Nov.) 1936.

8. Bergamini, Herbert, and Shepard, L. A.: Bilateral Atelectasis (Massive Collapse) of Lung, Ann. Surg. **86**: 35 (July) 1927.

and a questionable one reported by Santee [9] had come to light before the introduction of cyclopropane. Probably the added factors of quiet respiration and a high alveolar oxygen content have accentuated the possibility with cyclopropane. Actually the blood nitrogen brought to the alveoli and that of the supplemental and residual air are better preserved under the present methods of administering cyclopropane than under most previous methods of handling the older anesthetics.

Coryllos, in another paper,[10] discussed the two cases reported by Bergamini and Shepard. He explained them on the basis of rapid absorption by the lung of the quickly absorbable anesthetic gases plus bronchial obstruction, although the pathologists three years earlier were careful to state that no obstruction was present.

Nevertheless, that a rapid respiratory death from massive atelectasis following the administration of cyclopropane occurs occasionally is beyond question. That pulmonary morbidity after prolonged administration of cyclopropane is unduly greater than the otherwise very low incidence of this complication following cyclopropane anesthesia is suggested by figures from this hospital to be published shortly. The speculation involved, pending further investigation with animals, is whether the process of development follows the outline given here.

The following four cases represent examples of massive atelectasis following cyclopropane anesthesia:

Case 1.[11]—An ambulatory white woman, aged 31, who weighed 170 pounds (77 Kg.), was operated on for subacute pelvic inflammatory disease. Preliminary medication consisted of one-sixth grain (0.01 Gm.) of morphine and 1/150 grain (0.0004 Gm.) of atropine one hour before operation preoperatively. The administration of cyclopropane was started at 8:07. Three minutes later the patient was catheterized, and then she was draped for the operation. About eight minutes from the start of anesthesia, before the incision was made, the respirations gradually ceased and the pulse stopped. All attempts at revivification failed, and the patient was pronounced dead at 8:25. Attempts at resuscitation were continued for another half hour.

Autopsy showed bilateral massive collapse of the lungs. The trachea and the bronchi were clear and unobstructed. The right ventricle was dilated, and localized pelvic peritonitis was present.

This case, because of the marked bilateral atelectasis and the careful statement by the pathologist that no obstruction was present in the trachea or the bronchi, fits excellently into the general interpretation we have given to all these cases. However, the onset early in the course of the anesthesia is not typical, and the case differs in this respect from the others.

Case 2.[12]—A man, aged 20, was given cyclopropane by the endotracheal method for an operation on the stomach. The duration of anesthesia was one and one-half hours. The respiration volume was purposely maintained considerably below normal. The patient's condition was excellent at completion of the operation.

On his way back to the ward he showed cyanosis and labored breathing. Oxygen was called for, but the patient was dead within three minutes, before oxygen was made available.

Autopsy showed massive collapse of one lung.

Case 3.[12a]—A woman, aged 53, of average height and weight and in good physical condition, who was operated on for a small femoral hernia, was given one-sixth grain (0.01 Gm.) of morphine and 1/150 grain (0.0004 Gm.) of atropine about ten minutes before anesthesia started. Anesthesia began at 8:40 and the operation at 8:45; at 9:07 the operation and the anesthesia ended. Both operation and anesthesia were uncomplicated. The patient left the operating room in good condition, but by the time her room was reached she was cyanotic and showed labored breathing. Her condition became rapidly worse. Epinephrine and manual artificial respiration were given without avail. She was pronounced dead at 9:25.

Autopsy showed that the left lung was entirely dark red and noncrepitant. The right lung was aerated but dark red and congested, with patches of atelectasis. The trachea and the bronchi contained a slight amount of mucus but no plugs or obstruction. The right auricle and ventricle were engorged with blood and enlarged to twice their normal size.

Case 4 is our own. It occurred during the early months of our experience with cyclopropane and established a permanently cautious approach toward this anesthetic. No such interpretation as is here given was then attached to the occurrence. It was presumed to be a matter of an overdose, but even then this interpretation did not seem entirely satisfactory to explain what occurred.

Case 4.—Mrs. E. F., aged 35, of average height and weight, was operated on for excision of a rectovestibular fistula. Preliminary medication consisted of one-fifth grain (0.013 Gm.) of morphine and 1/150 grain (0.0004 Gm.) of atropine given at 8 a. m. Anesthesia started at 8:45 and ended at 9:33 (duration forty-eight minutes) and was uneventful.

When the mask was removed the pulse rate was 94, the respiratory rate 14 and the color good. The patient was placed on her side on a stretcher and started for her room accompanied by the anesthetist. By the time the elevator was reached, approximately three minutes after removal of the mask, the respirations were shallow and more rapid. Some cyanosis had become evident. The pulse was regular and of good quality. When the patient's floor was reached, respiration had completely stopped and the cyanosis was definite. The pulse was still good. Artificial respiration by a modified Schafer method was begun (the patient was on her side on a narrow stretcher) and the patient rushed back to the operating room. Rapidly flowing oxygen was delivered by tube into the posterior part of the pharynx while manual artificial respiration was being continued and a tightly fitting mask made ready. There was no obstruction to respiration, and a fair tidal volume was maintained by artificial respiration. The pulse remained good for about three minutes after total cessation of the respiration, but during the fourth minute it began to fail and became irregular. Cyanosis by this time was maximal and the patient's condition desperate.

At this point the patient gave an enormous convulsive gasp. This was followed shortly by the resumption of shallow rapid breathing. There was no relief of cyanosis at first, despite the breathing by this time of 100 per cent oxygen under efficient artificial respiration. Manual pressure on the bag, which had a tightly fitting face piece, was used to fortify the now resumed but shallow respirations. The pulse returned to an irregular but more forceful beat shortly after the resumption of spontaneous respiration. During another four minutes the cyanosis cleared somewhat, and in another minute the color was about normal. The patient regained consciousness in ten more minutes. Beyond a slight trace of cyanosis for the first twenty minutes, she had a completely uneventful recovery.

PREVENTION

If our speculation as to the cause of this type of postoperative massive collapse is correct, the obvious remedy is to add inert gas to the cyclopropane mixture. Neff and Stiles [13] have already suggested the advisability of diluting the cyclopropane atmosphere. They

9. Santee, H. E.: Bilateral Collapse of the Lung, Ann. Surg. **85**: 608 (April) 1927.

10. Coryllos, P. N.: Postoperative Pulmonary Complications and Bronchial Obstruction, Surg. Gynec. & Obst. **50**: 795 (May) 1930.

11. Dr. Antonio Rottino of St. Vincent's Hospital gave permission to report the postmortem observations in this case.

12. Quoted by permission of the publishers from Guedel, A. E.: Inhalation Anesthesia: A Fundamental Guide, New York, Macmillan Company, 1937.

12a. Dr. Thomas Dowd of the Hospital for Ruptured and Crippled gave us permission to report this case.

13. Neff, W. B., and Stiles, J. A.: Some Experiences with Cyclopropane Anesthetic, with Special Reference to the Diabetic Patient, Canad. M. A. J. **5**: 35-36 (July) 1936.

did not connect the idea of dilution with the prevention of atelectasis but were attempting to prevent the development of shock in operations of three or four hours' duration. They used nitrogen and nitrous oxide as diluents.

For the purpose of preventing atelectasis, the addition of nitrous oxide would serve little purpose, but nitrogen would be effective. Lemmer and Rovenstine have shown nitrous oxide to be absorbed almost as rapidly as oxygen and carbon dioxide.

The most useful addition to the cyclopropane atmosphere or other anesthetic atmospheres should be either hydrogen or helium. Both these gases, besides having more prolonged rates of absorption by the lung than nitrogen, have the added mechanical advantages for respiratory purposes inherent in light gases.

Helium for therapeutic purposes was conceived and introduced into medicine by Barach [14] and has since been adopted for anesthesia by Eversole,[15] among others. Eversole used helium in occasional cases chiefly to overcome spasm of the cords and other forms of respiratory obstruction. Saklad [16] advised its use in the treatment of failing respiration accompanying spinal anesthesia. Hydrogen, the lightest of all gases, may eventually prove to be the most valuable as an anesthetic, particularly if subsequent work confirms or enhances the claimed advantages of very light gases for respiratory purposes.

Helium, however, being light and inert and not explosive, seems at this time to be the best substitute for nitrogen in the replacement of that very necessary supporting gas in the pulmonary alveoli.

In Hershey's [17] experiments with animals, helium with oxygen in percentages of from 80 to 50 supported life as well as normal air over long periods and better than any other gas when mixed with adequate proportions of oxygen.

We therefore suggest the routine use of helium during the administration of cyclopropane or of any other anesthetic given in a high oxygen atmosphere that will tolerate dilution. Helium will not only replace the nitrogen which has been washed out of the alveoli and thus prevent the closure of the alveoli, with subsequent atelectasis, but will also bring to the anesthetic atmosphere the mechanical advantage of light gas for respiratory purposes.

The most convenient method for routine use is to establish anesthesia with a small bag content of gases.[18] Approximately enough helium to double the size of the bag is then added. This procedure leaves an adequate oxygen content in the bag. If one assumes that by this time the oxygen content in the bag approximates 60 per cent, the cyclopropane 25 per cent and other gases 15 per cent, then doubling the contents of the bag would leave the oxygen at 30 per cent. But with a low content a considerable amount of other gas and space enters into the calculations. Gas among the soda lime granules, in the face piece and in the supplemental and residual air is to be considered. The supplemental and residual air contains about 2,500 cc. The face piece and canister hold about 1,100 cc. Thus a total space of about 3,600 cc., besides the content of the bag, has to be considered. The individual spaces, while varying in their content of carbon dioxide, nitrogen, oxygen and cyclopropane according to their location, have in common, after the administration of cyclopropane, a higher than normal oxygen content.

Therefore, doubling the size of a "low" bag (containing to begin with about 1½ to 2 liters) is an effective way of supplying a sufficient percentage of helium to the mixture for the purposes suggested in this paper. When helium is used in this way and an allowance made for subsequent additions, the cost is kept low. This averages thus far in our experience about five cents per person anesthetized.

It is well to watch, however, for any sign of cyanosis after these additions. Any additions of helium after the first one should be considerably reduced in amount.

At present the additions of helium used at St. Luke's Hospital are unmetered. If it were desired, the amounts could easily be metered. But too great concern over the accuracy of the amounts added is pretense, as momentary consideration of the unknown and uncontrollable variables will show.

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THE IDENTIFICATION OF GONOCOCCI IN COMPLICATIONS OF GONORRHEA

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AND
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As a rule it is not difficult to establish a diagnosis of acute gonorrheal infection; however, the diagnosis of chronic lesions and of complications often remains obscure. The spread of the initial infection to the deeper tissues and to other parts of the body requires dependable and complete bacteriologic studies. Many of the complications of gonorrhea, such as arthritis, gonococcemia and endocarditis, as well as perigenital lesions, have often remained undiagnosed, largely because heretofore little attempt has been made to recover the organism. The reason for failure in diagnosis is twofold: (1) A complication may occur so late that the underlying disease is not suspected and (2) it is a general belief that the gonococcus is difficult to recover and to identify. It is our purpose to illustrate the necessity of making certain of the diagnosis when complications of gonococcic infections are involved and to show that bacteriologic procedures of proved value, which are relatively rapid and simple in performance, are now available for more widespread clinical use.

During the past five years we have recovered the gonococcus from blood, synovial fluid, pus from tendon sheaths, material from cutaneous lesions, peritoneal fluid, fluid from an abdominal cyst, material from ovarian and Bartholin glands and material from labial, periurethral and perianal abscesses. We have in many instances cultured the gonococcus from cervical, urethral or prostatic discharges when examination of smears gave negative or inconclusive results. In fourteen of twenty-five cases of proved gonorrheal arthritis

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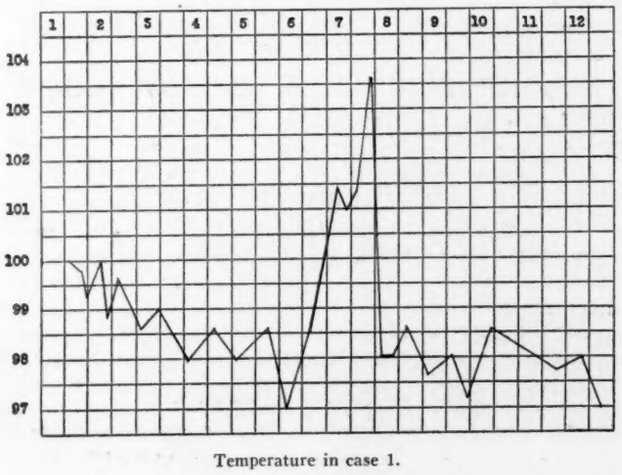
the history did not indicate previous gonococcic infection, and in these cases either the routine smear was reported to be negative or no urethral or cervical discharge was obtainable. The diagnoses were made by recovering the organisms from blood (in seven cases), synovial fluid (in sixteen cases) or both (in two cases).

ARTHRITIS AND BACTEREMIA WITH SUBSEQUENT RECOVERY

Four patients had arthritis and bacteremia and subsequently recovered. In two of these the invasion of the blood stream appeared to be a transient complication which occurred suddenly in the course of moderately severe arthritis and was characterized by an abrupt rise and return to normal of the temperature. A report of one case is presented:

CASE 1.—P. F., a housewife, aged 25, had been admitted to the hospital two years previously for cauterization of the cervix, bilateral salpingectomy, right oophorectomy and appendectomy, after which she became well. The present illness began with chills, fever, nausea and pains generalized throughout the body. When she was admitted to the hospital two days later, the temperature was 100 F. and the pulse rate 90. There were



Temperature in case 1.

tenderness, pain and slight swelling in the metacarpophalangeal joint of the first digit of the right hand and over the extensor tendons of the dorsal aspects of the left foot and the left knee. After the initial chill a hemorrhagic vesicle developed above the left external malleolus, which two weeks later showed a necrotic center containing pus. Three days afterward vesicles developed on the lateral aspect of both thighs and on the inferior aspect of the right internal malleolus. Two days later a small lesion developed over the left biceps.

On the seventh day after the patient's entry, coincidentally with a sudden rise in temperature to 103.6 F., a large lesion with a necrotic center appeared over the lateral aspect of the right foot, and blood taken at that time for culture showed a growth of gonococci. Within one week the lesion on the foot was 3 cm. in diameter, and in its center was a flat pustule 1 cm. in diameter, covered with a transparent epidermis which enclosed a small amount of rapidly drying purulent material. The material aspirated from the pustule did not show any organisms in the smear or by culture. The temperature returned to normal on the eighth day and continued so during the remainder of the patient's stay in the hospital, which was uneventful.

The other two attacks of gonococcic arthritis with bacteremia were more severe; however, both patients recovered. One case is of interest because of the difficulty in diagnosis and is presented in brief:

CASE 2.—J. G., a married woman, aged 52, was well until two days previous to entry, when she got wet while walking in the rain. During the following night she awakened from sleep with severe chills, profuse sweating and generalized pain in all her limbs. On the following day she complained of pain in her left shoulder and right wrist. Her past history did not show any evidence of previous gonococcic infection. Early in her married life she had had one pregnancy, which had been terminated by abortion. At the time of entry she had known for three years that she had an abdominal tumor. She gave a history of menstrual irregularity and profuse bleeding for the past two years.

On pelvic examination the staff gynecologist found a mass which was considered to be a multilobular leiomyoma of the uterus or possibly an ovarian cyst. A later examination indicated that the patient might have an old adherent tubo-ovarian lesion, but this was not thought to be the focus of her present infection. No vaginal discharge or cervical lesion was present. Smears and cultures of material from the cervix were negative for gonococci. At the time of entry, the patient had a temperature of 102 F. and a pulse rate of 90. She had pain in her left shoulder and right wrist and pain and swelling of the left little finger. There were erythematous areas over the surface of the right foot. Five days after entry the left wrist and elbow and both ankles became involved with pain and swelling, and a red swollen fluctuant lesion appeared over the right ulnar surface of the forearm; this lesion, which disappeared after several days, was considered to be possibly metastatic.

On the patient's twenty-first day in the hospital, a blood culture was made, from which gonococci were recovered. On the twenty-eighth day about 3 cc. of fluid was aspirated from the right wrist; a smear was not made, but gonococci were recovered by culture. At the time the blood culture was made, pustular cutaneous lesions appeared on the knuckles, the right elbow, one thumb and the soles of the feet. Four days later material from the pustule on the thumb was aspirated and cultured, but gonococci were not observed. The patient was given pyrotherapy and recovered.

ENDOCARDITIS, BACTEREMIA AND ARTHRITIS

Gonococcic endocarditis is considered a rare complication. We have been successful in recovering the organism in five cases by culture during life, and in three cases the endocarditis was confirmed at necropsy. We believe that the incidence of gonococcic endocarditis, like that of gonococcic arthritis and gonococcemia, would be found to be greater than is suspected if, in clinical and postmortem studies, greater effort were made to recover the organism. We present a case of endocarditis which was unusual because the diagnosis was made by observing gonococci first in a cutaneous lesion:

CASE 3.—S. P., a white man, aged 48, became acutely ill with chills, fever and general malaise seven days before entering the hospital. On the second day of his illness a rash appeared on his body and extremities; on the third day several joints became painful, particularly the left wrist, which was swollen. He gave a history of having had gonorrhea at the ages of 16 and 18, but he had had no recent urethritis. Examination showed a maculopapular eruption over the extensor surfaces of the arms, thighs and buttocks and on the left elbow and the left thigh. Individually, the lesions varied considerably in size and in stage of development. There was marked conjunctivitis; there were hemorrhages in the gums, on the labial grooves and in the mouth, nose and throat, and the tonsils were swollen. The heart showed no abnormalities. The Wassermann reaction of the blood was positive. A small nodular mass was found along the course of the urethra; there was no discharge. The patient had a definite swelling, with redness and tenderness, of the left wrist.

On the day after his entry into the hospital, the left knee became painful. On the third day, a number of bullae appeared in the skin over the buttocks and the ankles; cultures of pus from one of these showed gonococci. These lesions later became pustular, leaving necrotic centers. Cultures of blood taken on the second and the tenth day showed growths of gonococci. The patient rapidly became very ill and almost comatose. His temperature remained between 101 and 103 F., and the pulse rate was from 110 to 130. At no time was there any clinical sign of endocarditis, and the spleen was not palpable.

The patient was given pyrotherapy, and after the first treatment his condition seemed slightly improved. However, on the thirteenth day in the hospital his temperature rose to 105.4 F., his pulse rate was 120 and his respiratory rate was 52. He expectorated thick, yellowish mucus and perspired freely. During the next day his condition became rapidly worse; his temperature was 105.8 F., his pulse rate 140 and his respiratory rate 40. Rales were present at both bases, and rigidity of the extremities and stiffness of the neck were marked. No murmurs were noted on examination of the heart, and the spleen was not felt. The patient died on the fourteenth day of his stay in the hospital.

Necropsy showed subcutaneous hemorrhages; the bullae in the skin had disappeared, and there were fresh hemorrhages in the abdominal muscles and lungs. There were adhesions around the ascending colon and around the liver. The capsule of the liver was thickened, no cirrhosis was evident and the gallbladder was normal. On gross and microscopic examinations, the urethra and the prostate were found to be normal. The spleen was moderately enlarged. There were no alterations in the myocardium; the mitral valve showed a slight endocarditic patch. There were aortic-verrucous endocarditis and typical acute endocarditis.

It is interesting that of the nine patients with gonococcemia, four had cutaneous manifestations. In only one of three attempts were we successful in recovering the organism from cutaneous lesions. Clinically there appears to be a time relationship between the occurrence of bacteremia and the development of cutaneous manifestations. The cutaneous lesions that are discrete and have pustules or necrotic centers are probably metastatic, as was proved in case 3. Klein [1] reported the recovery of gonococci from the cutaneous lesions of a patient with gonococcic arthritis. This is, as far as we know, the only other case reported in the literature in which gonococci were recovered from the cutaneous lesions.

Mention is made here only briefly of the remaining four cases of gonococcic endocarditis, bacteremia and arthritis. In the case of C. M., on examination no evidence was found of gonococcic infection, and clinically there was only presumptive evidence of gonococcic arthritis and endocarditis. One week before the patient's death the blood culture showed a growth of gram-negative diplococci which, morphologically and culturally, resembled gonococci, although complete identification was not made. At necropsy acute mural endocarditis, with mycotic aneurysm of the left ventricle and secondary involvement of the mitral and aortic valves, was observed. A smear of pus from a mediastinal abscess showed gram-negative diplococci. In the case of L. D., the diagnosis was made from the clinical signs of endocardial involvement, a positive smear of material from the cervix and a positive blood culture; the postmortem diagnosis was diffuse verruciform aortic valvulitis, fibrinous purulent endocarditis, chronic endocervicitis, chronic salpingitis and purulent vaginitis. In the case of R. W., the blood culture was positive simultaneously with the development of clinical signs of endocarditis. No necropsy was made. In the case of S. B., the diagnosis was made by clinical evidence of gonococcic infection and endocarditis, together with repeatedly positive blood cultures.

BACTERIOLOGY

Blood Cultures.—In culturing for gonococci, we used hormone-brain broth (hormone-heart-gelatin added to pieces of sterile brain, prepared by the medium department of the University of California Hospital). Nearly all pathogenic bacteria can be recovered from blood and other specimens by its use. However, some of the strains of gonococci grew more rapidly in brain-heart infusion (Difco) with the addition of from 30 to 50 per cent of sterile ascitic fluid. Usually both broths were used; 10 cc. of blood was inoculated directly into 200 cc. of each broth, which had been warmed previously. In one instance a specimen was collected into the hormone-brain broth at room temperature, and incubation was not begun for four hours after inoculation. Gonococci were recovered also from specimens of blood collected into 4 cc. of sterile 2.5 per cent sodium citrate solution and brought to the laboratory for inoculation into the mediums. According to our experience, the optimum time for taking the specimen of blood is when the patient's temperature is at the peak of a rise.

Even though examinations of the original cultures were made daily by means of gram smears, the cocci often were not observed until the fourth or fifth day. When about 0.5 cc. of the original culture was transplanted after twenty-four hours' incubation to 5 cc. of ascitic fluid-infusion broth, good growth of gonococci was found in the subculture after only twenty-four hours' incubation.

Synovial Fluid and Other Exudates.—The technic for culturing synovial fluid was the same as that used for blood. Gonococci were recovered from two specimens of fluid or pus on swabs which had been kept at room temperature for from fifteen to eighteen hours; the growth seemed to be markedly retarded, however, since it did not appear before the fourth day of incubation. Second specimens from the same patients were inoculated directly, and growth appeared in twenty-four hours. Swab specimens must not be allowed to dry during the interval after they are taken and before the inoculation; placement in an incubator during this interim is entirely contraindicated because of the rapid desiccation. The organisms were seldom observed in the direct smears of the original fluid or pus.

For isolating the gonococcus from discharges containing mixed flora, such as specimens of cervical, urethral or prostatic discharges, pus from perianal abscesses and specimens of urine, the McLeod [2] oxydase method has proved satisfactory. A brief description of the method is as follows: Inoculation is made on 10 per cent heated blood agar plates; incubation is carried out in a jar containing 8 per cent carbon dioxide for eighteen hours and out of the jar for an additional twenty-four hours. Then the surface of the plate is flooded with a 1 per cent aqueous solution of tetramethyl-paraphenylenediamine hydrochloride, which is allowed to drain off. Colonies having a positive oxydase reaction will turn bright purple within a few seconds; other colonies will become light blue or remain unchanged. Colonies with a positive oxydase reaction, which consist of gram-negative cocci and diplococci, are considered to be gonococci. The indicator allows the organisms to remain viable for thirty minutes, so that they may be picked off for further identification whenever this is indicated.

In our modification of the McLeod method, the medium employed is simpler and more adaptable for

1. Klein, H. M.: Studies on the Shwartzman Reaction: Hitherto Undemonstrated Antitoxins in Man, J. Infect. Dis. **52**: 312-327 (Nov.-Dec.) 1933.

2. McLeod, J. W.; Coates, J. C.; Happold, H. C.; Priestly, D. P., and Wheatley, B.: Cultivation of the Gonococcus as a Method in the Diagnosis of Gonorrhea with Special Reference to the Oxydase Reaction and to the Value of Air Reinforced in Its Carbon Dioxide Content, J. Path. & Bact. **39**: 221-231 (July) 1934.

use in small laboratories whose facilities do not permit the making of intricate mediums in small quantities. The procedure is as follows: 1. Enough brain-heart infusion (Difco) is added to brain-veal agar (Difco) to make the agar content 1.2 per cent instead of the usual 1.5 per cent. This medium is made up in double strength and sterilized in the usual manner. 2. Dehydrated hemoglobin (Difco) is made up in a 2 per cent solution as directed on the bottle and is sterilized. 3. An equal quantity of this heated sterile hemoglobin solution is added to the double strength melted agar; the mixture is then allowed to cool to 50 C., and the plates are poured. The plates should be used on the same day.

Gonococci appear to grow equally well on the two agars with or without the addition of the 8 per cent carbon dioxide. Usually the incubation under the increased carbon dioxide is eliminated; however, the plates are placed in a sealed jar for the first eighteen hours' incubation in order to give the medium an atmosphere which is increased in moisture content. Additional moisture is always kept in the incubator; the temperature for all the cultures for gonococci is maintained at 36.5 C.

Identification of the Gonococci.—We relied for identification of the organisms on fermentation reactions and on agglutination with diagnostic serum. The preparation of the medium for the sugar fermentation reactions is as follows: A pure culture of the organisms is inoculated by means of a pipet, a broth culture being used, on plates containing sugar-free agar with a hormone base, 30 per cent sterile ascitic fluid, 1 per cent dextrose or maltose and 1 per cent Andrade's indicator. Growth usually appeared in twenty-four hours, but fermentation was usually not in evidence before from forty-eight to seventy-two hours. Hiss serum water, which is often used to test fermentation reactions of streptococci and pneumococci, does not give satisfactory results; only one strain out of ten which were inoculated in it produced fermentation, although all gave reactions on the other mediums. These plates were not placed in jars but were incubated in the usual manner.

Agglutination with antigonococcus diagnostic serum confirmed the identification of sixteen strains. Dr. A. P. Krueger, associate professor of bacteriology, University of California, performed the agglutination tests.

SUMMARY

No attempt was made to carry out an intensive clinical or bacteriologic study or to present a complete bibliography.[3] We have presented our results in the culturing of gonococci in gonorrhea and some of its complications such as endocarditis, bacteremia, and other metastatic lesions. The bacteriologic procedures that we have outlined aided greatly in diagnosis and therefore were of clinical value in selecting proper therapeutic measures.

3. An excellent bibliography is contained in the "Report of the Committee for Survey of Research on the Gonococcus and Gonococcal Infections," prepared by Ruth Boring Thomas and Stanhope Bayne-Jones, supplement to the American Journal of Syphilis, Gonorrhea and Venereal Diseases, January 1936.

Store Food and Store Teeth.—Let us cease pretending that tooth brushes and tooth paste are any more important than shoe brushes and shoe polish. It is store food which has given us store teeth.—Hooton, E. A.: Apes, Men, and Morons, New York, G. P. Putnam's Sons, 1937, page 263.

Clinical Notes, Suggestions and New Instruments

SERUM CARDITIS: THE MORPHOLOGIC CARDIAC ALTERATIONS IN MAN ASSOCIATED WITH SERUM DISEASE

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In a recent report from Bellevue Hospital [1] two instances were described in which patients received large doses of antipneumococcus serum and came to necropsy four and nineteen days, respectively, following signs of serum disease. The structural alterations in these cases consisted of proliferation of histiocytes in the mural and valvular endocardium and in the intima of the aorta, pulmonary and coronary arteries, accompanied by multiplication of the interstitial cells of the myocardium and other viscera. Necrotizing arteritis and periarteritis of the smaller coronary arteries was a prominent feature in one case. It was felt that the composite picture is unlike that of any disease heretofore described. The coexistence of these lesions with clinical evidence of serum disease

Fig. 1.—Section of the left ventricle showing dense, diffuse, cellular thickening of the endocardium over the columnae carneae.

and their similarity to those found in animals with protracted anaphylaxis induced by foreign serums [2] led the authors to suggest that these alterations are of hyperergic nature and related to the administration of foreign serum.

Recently, while studying the visceral lesions of anterior poliomyelitis in the Bellevue Hospital laboratories, Dr. Einar Gustafson [3] encountered a case from the 1931 epidemic which he called to my attention. This case offers further proof that structural alterations in the heart may accompany serum disease in man.

REPORT OF CASE

R. M., a white youth, aged 20, admitted to the Fourth Medical Division of Bellevue Hospital July 7, 1931, complained of headache, drowsiness and stiffness of the neck of four days' duration. Physical examination revealed rigidity of the neck, bilateral Kernig sign, and incoordination and weakness of the

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1. Clark, Eugene, and Kaplan, B. I.: Endocardial, Arterial and Other Mesenchymal Alterations Associated with Serum Disease in Man. Arch. Path. **24**: 458 (Oct.) 1937.

2. Klinge, F.: Beitr. z. path. Anat. u. z. allg. Path. **83**: 185, 1930. Vaubel, Ernst, ibid. **89**: 374, 1932. Apitz, Kurt: Virchows Arch. f. path. Anat. **289**: 46, 1933. Junghans, E.: Beitr. z. path. Anat. u. z. allg. Path. **92**: 467, 1933.

3. Gustafson, Einar, to be published.

right lower extremity. The temperature was 103 F., the pulse 112 and the blood pressure 114 mm. of mercury systolic and 90 diastolic. The spinal fluid showed 180 cells with 76 per cent polymorphonuclear leukocytes and 24 per cent monocytes; culture of the spinal fluid was sterile and the spinal Wassermann reaction was negative.

Soon after admission the patient was apathetic, but in the next few days he became alert. July 11, right external rectus weakness and flaccid paralysis of all limbs, more marked on the right, were observed. During these four days the patient's temperature did not rise above 101 F. and the pulse varied from 90 to 100 per minute. The spinal fluid cell count diminished and the cells were chiefly of the mononuclear type.

July 11, 20 cc. of concentrated horse serum was administered intraspinally and an equal amount was given intramuscularly.

During the following week apathy returned, right lower facial weakness developed and breathing became thoracic in type. The temperature rose to 102.6 on the 13th and maintained a level of from 103 to 104 F., with the pulse between 120 and 130. The white blood count July 13 was 16,800 per cubic millimeter with 92 per cent polymorphonuclear leukocytes; July 18 it was 22,400 per cubic millimeter with 84 per cent polymorphonuclear leukocytes, 13 per cent lymphocytes, 2 per cent transitionals and 1 per cent eosinophils. A transfusion of 300 cc. of whole blood was given July 14 without reaction. The spinal fluid remained sterile.

July 17 an erythematous rash was noted over the entire body, petechiae over the trunk and arms, edema of the left lid and marked enlargement of the cervical, inguinal and axillary lymph nodes. A blood culture taken at this time was sterile after five days' incubation.

July 18, tympanites and difficulty in respiration were noted. The patient was placed in a respirator. In the following twelve hours the pulse became weaker and irregular. The temperature rose to 107 F., the pulse became impalpable and death occurred July 19.

POSTMORTEM EXAMINATION

Necropsy was performed a few hours after death. Alterations were not observable by naked eye in the thoracic or abdominal viscera. The brain appeared unaltered, but the spinal cord showed congestion, edema and punctate hemorrhages.

Microscopic Changes.—Brain and Spinal Cord (described by Dr. Lewis Stevenson): Sections of the medulla, cervical and thoracic cord showed typical lesions of acute anterior poliomyelitis, with marked lymphocytic exudate about the blood vessels and in the substance of the anterior horns. The latter also showed necrosis of nerve cells and a few minute hemorrhages. There was a slight lymphocytic infiltration in the pia arachnoid.

Heart: Paraffin sections of three blocks of tissue removed from the left ventricle were available for study. There were no sections of the valves, larger coronary arteries or aorta.

The myocardial alterations were characterized by dense, diffuse, cellular infiltration and edema of the mural endocardium, particularly over the columnae carneae and the mouths of the thebesian veins (fig. 1). The lining endothelial cells were sometimes intact and sometimes invisible but there were no thrombotic deposits or vegetations. The cells were predominantly of the histiocytic type, oval, polyhedral or fusiform, varied in size from 10 to 40 microns, and possessed abundant, lightly basophilic cytoplasm. A few lymphocytes and eosinophilic and neutrophilic polymorphonuclear leukocytes were also found. Accompanying this reaction in the endocardium was a focal infiltration of similar cells in the intermuscular connective tissue, around the interfascicular arteries, capillaries and venules, between the muscle fibers and beneath the epicardium (fig. 2). Though the arteries and arterioles were frequently surrounded by histiocytes, the walls of the vessels were unaltered. There were no lesions that resembled Aschoff bodies.

Liver: There was slight focal infiltration of histiocytes in the perilobular areas.

Kidneys: Slight infiltration of histiocytes was visible around some of the glomeruli.

Spleen: There were several foci of hyperplasia in which large mononuclear cells with basophilic cytoplasm predominated.

Lymph Nodes: The architecture of the nodes was preserved but the sinuses were crowded with large mononuclear cells.

Other Organs: The lungs showed edema and congestion. The other viscera were not examined microscopically.

SUMMARY

A youth, aged 20, with acute anterior poliomyelitis affecting all limbs and the muscles of respiration, died twelve days after the onset of the disease. Seven days before death, 40 cc. of concentrated horse serum was administered. Two days prior to death, signs of serum disease appeared. Postmortem study disclosed, in addition to the microscopic appearance of acute anterior poliomyelitis, diffuse infiltration of histiocytes in the subendocardial and connective tissues of the heart accompanied by focal infiltration between the muscle fibers.

COMMENT

According to Landon and Smith,[4] cardiac lesions of the nature exhibited in the case reported have not been observed in epidemic poliomyelitis. This, fortified by the absence of sepsis, and the similarity of these lesions to those observed in animals during protracted serum anaphylaxis,[2] and in the two previously reported cases of serum disease in human beings, lead to the belief that the cardiac alterations in this case are morphologic reactions to horse serum. The existence of serum disease in this patient, as well as in the two patients previously referred to, and the absence of these lesions in those serum-treated individuals in whom serum sickness did not develop,[1] support the suggestion that such alterations represent the morphologic expression of a hyperergic state associated with serum disease. The focal histiocytic infiltration of the liver and kidneys, although milder than in the two other cases, is probably of the same nature.

Fig. 2.—Section of the left ventricle showing cellular infiltration along the intermuscular tracts, lining of thebesian veins and between the muscle fibers.

In the two cases described in the first report, antipneumococcus serum was given several times a day over seven and eleven days respectively, with a corresponding serum volume of 600 and 2,000 cc. The case here reported indicates, however, that this morphologic reaction may follow a single injection (combined intraspinal and intramuscular) of a relatively small amount of serum (40 cc.). The serum employed was "concentrated horse serum," which may be equivalent to many times its volume of serum refined for its specific immunologic properties.

The structural alterations in the case here reported differ from one of the other two in the absence of necrotizing arteritis

4. Landon, J. F., and Smith, L. W.: Poliomyelitis, New York, Macmillan Company, 1934.

of the coronary arteries. It is not possible to determine the factors responsible for the occurrence of the latter lesion. In the case in which it was observed, death occurred nineteen days after the appearance of serum disease, whereas in the two other cases four and two days, respectively, elapsed between the appearance of serum disease and death.

Cases are too few to permit any conclusion concerning the functional significance of these lesions. In the three cases thus far studied, the underlying disease appears to explain the clinical phenomena and the fatal outcome.

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A CASE OF INTESTINAL HETEROPHYIDIASIS OF MAN IN HAWAII

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Intestinal heterophyid infestation has been reported in man from various parts of the world, including China, Japan, Korea, the Philippines, Egypt and the Balkan states, in areas where parasitized fish is eaten raw or uncooked. Recently a case of heterophyidiasis has been discovered in man in Hawaii, and the source of infestation is believed to have been infested raw fish, possibly mullets, which the patient had eaten. This finding marks a new geographic endemic area for this group of parasites; this new distribution would have been expected because of the large number of Chinese, Japanese and Filipinos who have migrated to Hawaii and because of the presence of melanid snails and mullet, which have been reported in other localities as serving as primary and secondary intermediate hosts respectively of these parasites. It is not surprising also to find human infestation in Hawaii, since raw fish is customarily eaten by certain racial groups residing here.

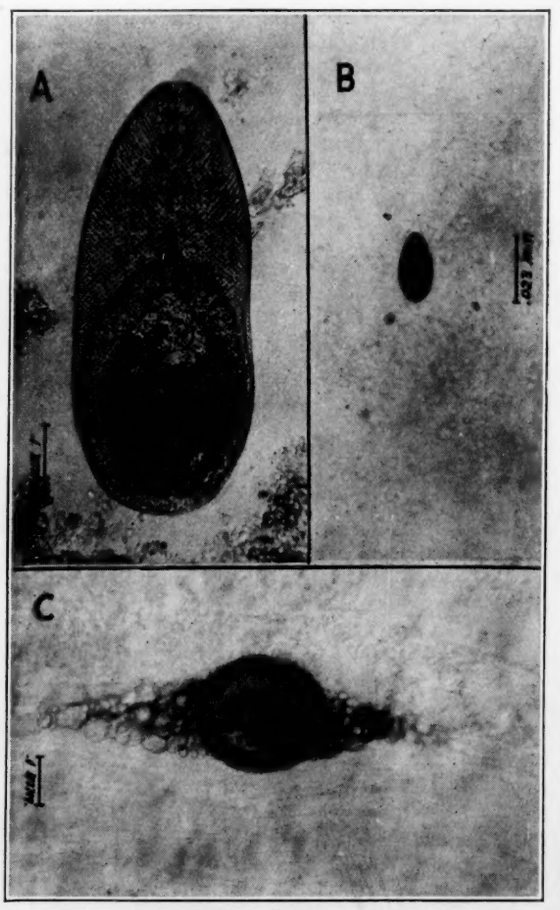
Heterophyid flukes as adults are extremely small, often only about 0.5 mm. long. Several species have been reported from man; Heterophyes heterophyes was the first member of this group, found by Bilharz in 1851 in the small intestine of a boy in Egypt; since then many other species have been reported from the intestinal tract of carnivorous mammals, birds and fishes. In 1911 Kutsurata described Metagonimus yokogawai, which was the first of these flukes to be found in man in the Orient. Africa and Garcia [1] in 1935 reported the finding of Monorchotrema taichui, Diorchitrema pseudocirrata (= Stellantchasmus falcatus) and Heterophyes brevicaeca in man in the Philippines; the first two species were also found in dogs.

Heterophyids in man have been reported as causing little disorder, and the clinical symptoms due to their presence are often negligible. In 1935 Africa, de Leon and Garcia [2] reported that these flukes parasitize the intestinal mucosa, and, because of an unbalanced parasitic relationship between the human host and these worms, the latter wander into the deeper layers of the intestinal wall, become imprisoned and die; the ova in the bodies of these flukes that degenerate are taken up by the lymphatic or blood streams and are carried to various parts of the body, including the brain and heart. Africa and his associates [3] have reported heterophyid ova in acute lesions of the myocardium of several individuals, and these ova were believed to be instrumental in bringing about fatal acute heart attacks; they also suggest that the cardiac beriberi often noted in the Far East, where the eating of raw fish is common and heterophyid infestations are endemic, are possibly cases of cardiac heterophyidiasis.

REPORT OF CASE

A. N., a man, aged 26, Japanese, was referred to one of us (O. L. S.) June 27, 1937, for diagnosis. The patient was a trainer of polo ponies and worked on a ranch at Mokoleia, Island of Oahu, T. H. He was born and reared here and never traveled away from the islands. His past history indicated only a severe attack of influenza in 1918, lasting a few weeks, which was followed by a good recovery.

Six weeks before he was seen, diarrhea suddenly developed, for which he could not account. When he continued to have from six to ten loose stools daily for several days he consulted a physician, but apparently only symptomatic treatment was offered and gave him no relief. The diarrhea persisted for about three weeks, during which time he lost his appetite, his body weight dropped from the average level of from 142 to 144 (64.4 to 65.3 Kg.) down to 123½ pounds (56 Kg.), and he had a corresponding loss in body strength; during that time he had shown absence of urinary symptoms, nausea, vomiting, melena and fever. When first seen he was no longer having diarrhea



A, adult heterophyid, Stellantchasmus falcatus, recovered from the intestine of a cat fourteen days following experimental feeding of an infested mullet; *B*, egg of the parasite found in the feces of the cat; *C*, encysted metacercaria of this fluke in the musculature of an infested mullet.

but complained of a "nervous feeling" and discomfort over the area corresponding to that of the colon, and particularly the right upper quadrant. The pain was not acute but was constantly present as a discomfort which was not influenced by the intake of food, evacuation of the bowels or mechanical pressure. Inquiry into his habits brought out the fact that he was a moderate smoker and drank beer occasionally. His hygienic surroundings were good; he lived in a house fitted with modern equipment and his meals included fresh vegetables, milk, eggs and the like; the water supply was from an artesian well on the ranch. He also admitted further being fond of certain kinds of raw fish, which he ate with his regular meals;

1. Africa, C. M., and Garcia, E. Y.: Heterophyid Trematodes of Man and Dog in the Philippines with Descriptions of Three New Species, Philippine J. Sc. **57**: 253 (June) 1935.

2. Africa, C. M.; de Leon, W., and Garcia, E. Y.: Heterophyidiasis: IV. Lesions Found in the Myocardium of Eleven Infested Hearts Including Three Cases with Valvular Involvement, Philippine J. Pub. Health **3**, Nos. 1-2 (March-June) 1936; III. Ova Associated with a Fatal Hemorrhage in the Right Basal Ganglia of the Brain, J. Philippine Islands M. A. **16**: 22 (Jan.) 1936.

3. Africa, C. M.; de Leon, W., and Garcia, E. Y.: Heterophyidiasis: II. Ova in Sclerosed Mitral Valves with Other Chronic Lesions in the Myocardium, J. Philippine Islands M. A. **15**: 583 (Nov.) 1935; Intestinal Heterophyidiasis with Cardiac Involvement: Contribution to the Etiology of Heart Failures, Philippine J. Pub. Health **2**, Nos. 1-2 (March-June) 1935.

also when he went into a beer hall for a drink he would frequently eat a "Japanese salad," consisting of raw fish, raw lettuce and soya sauce. He did not know the kind of fish served in the beer halls, but at the ranch he ate largely raw "fresh-water" mullet and occasionally a local fish which he called "Chinese cat-fish." He could not date the onset of illness with any particular intake of raw fish.

The patient's physical examination on the first visit was as follows: temperature, 98.6 F.; pulse, 70; blood pressure, 132 systolic, 80 diastolic; weight, 123½ pounds. The urine showed only a few scattered pus cells and a few shreds of mucus. A careful physical examination failed to reveal any other noteworthy changes. The clinical impression was that he harbored some intestinal parasite, possibly amebas, and he was advised to enter a hospital for a more thorough study. The following day he entered Queen's Hospital.

Further examination revealed the urine negative, stool negative for amebas, guaiac test negative for occult blood. Blood: hemoglobin 75 per cent, red blood cells 4,956,000, white blood cells 9,100, polymorphonuclear leukocytes 47 per cent, eosinophils 2 per cent, small lymphocytes 44 per cent, basophils 7 per cent. The Weil-Felix test for typhus fever gave a negative agglutination in all dilutions. The Widal test gave a negative agglutination in all dilutions for B. typhosus, paratyphosus A and paratyphosus B. Undulant fever agglutination was negative in all dilutions. The Wassermann and Kahn reactions were negative. The white blood count July 3 still showed a peculiar shift in the differential: white blood cells 7,100, polymorphonuclears 37 per cent, eosinophils 4 per cent, monocytes 12 per cent, small lymphocytes 47 per cent.

A gastro-intestinal study revealed the following: Fluoroscopy of the chest was negative. Plain plates of the kidney, ureter, bladder and gallbladder were negative. A barium sulfate meal showed nothing unusual about the esophagus. The stomach was ptotic. No constant stomach or cap deformities could be found. At six hours there was no delayed emptying of the stomach. At twenty-four hours the colon was partially filled with barium, as was the appendix, which looked normal and was not tender to pressure. A barium enema was negative. X-ray diagnosis was negative, except for some colon irritability.

Studies of the stool were made daily, both from the normal evacuation and after saline purges. The presence of amebas was not found at any time, but small fluke ova from 0.023 to 0.025 mm. long by 0.011 mm. wide were noted (*B* in the accompanying illustration). With the finding of these ova he was put on a temporary starvation with purgation followed by 6 Gm. of oleoresin of aspidium, which was given July 6 in divided doses and with no toxic manifestations. He had several watery stools after treatment, and examination of these stools revealed several hundred tiny flukes about 0.6 mm. long by 0.2 mm. wide, which, although partially degenerated, could be identified as belonging to the genus Stellantchasmus and closely related, if not identical, with Stellantchasmus falcatus Ouji and Nishio, 1916 (syn. Diorchitrema pseudocirrata Witenberg, 1929). Following one dose of aspidium the patient began to feel better and was relieved of further symptoms of distress over the colon, his appetite returned and he gained about 3 pounds (1,360 Gm.) in the next week. Daily examination of the stool revealed a few ova for two days following the treatment, which then disappeared entirely. July 15, when he was discharged from the hospital, the blood count had shown a distinct shift toward normal, being as follows: white blood cells 5,100, polymorphonuclear leukocytes 72 per cent, eosinophils 2 per cent, small lymphocytes 20 per cent, monocytes 6 per cent.

The finding of heterophyid flukes in the patient suggested that local mullet was the carrier of the parasite. Examination of six mullets (Mugil cephalus) caught in an enclosed ocean fish pond near Waialua Bay, Oahu, revealed all to be infested with a large number of fluke larvae (metacercariae) encysted in the musculature (*C* in the illustration). Five additional mullets, caught in the ocean in the Waialua Bay, were also found to be infested; one mullet weighing 265 Gm. was so heavily infested that in 1 gram of muscle there were counted 263 larvae. The cysts in the musculature measured about 0.25 mm. long by 0.19 mm. wide and enclosed a larva partially coiled on itself. Larvae that were dissected from cysts measured about 0.27 mm. long by 0.12 mm. wide and resembled morphologically the adult flukes recovered from the stool of the aforementioned patient, with the exception of size and development of the genitalia. This finding was verified by the feeding of the raw mullet to three young cats. In the course of two days diarrhea developed in all the cats, and on the fourth day one died; at autopsy there were found in the small intestine a large number of heterophyid flukes (Stellantchasmus falcatus) about 0.3 mm. long with developing ova in the uteri. A daily fecal examination of the other two cats revealed eggs of the flukes passing out on the tenth day following experimental feeding. One of these two cats was killed fourteen days following experimental infestation and a large number of the adult heterophyid flukes (*A* in the illustration) about 0.55 mm. long were recovered from the intestinal tract.

SUMMARY

1. This is the first case of heterophyid fluke in man reported from Hawaii and suggests a new endemic focus of the disease.

2. The source of the infestation was definitely traced to a species of mullet which abounds in the waters about Hawaii and which is frequently used for food.

3. Animal experimentation proved the pathogenicity of this fluke for cats.

4. A cure was apparently effected in the human being by the simple use of oleoresin of aspidium.

DUODENAL ULCER AS A CAUSE OF DEATH IN A CASE OF MENINGOCOCCIC MENINGITIS

CARL A. HARTUNG, M.D., CHATTANOOGA, TENN., AND JOSEF WARKANY, M.D., CINCINNATI

Duodenal ulcer in childhood has frequently been described. The literature has been reviewed by Holt,[1] by Veeder[2] and in 1919 by Theile,[3] who collected 125 cases. Although additional cases[4] have been reported since Theile's monograph appeared, his classification of the subject can still be considered valid. The majority of ulcers in early life occur in newly born infants suffering from melena neonatorum and in marantic infants. In older children trauma of the gastro-enteric mucous membranes,

From the Departments of Pathology and Pediatrics, University of Cincinnati College of Medicine, and the Contagious Disease Wards of the Cincinnati General Hospital.

1. Holt, L. E.: Duodenal Ulcers in Infancy, Am. J. Dis. Child. **6:** 381 (Dec.) 1913.

2. Veeder, B. S.: Duodenal Ulcer in Infancy, Am. J. M. Sc. **148:** 709, 1914.

3. Theile, P.: Ueber Geschwürsbildungen des Gastro-Duodenaltractus im Kindesalter, Ergebn. d. inn. Med. u. Kinderh. **16:** 302, 1919.

4. These include:
von Bosanyi, A.: Neuere Beiträge zur Pathogenese der Duodenalgeschwüre im Kindesalter, Jahrb. f. Kinderh. **97:** 182 (Feb.) 1922.
Paterson, D. H.: Duodenal Ulcer in Infancy, Lancet **1:** 63 (Jan. 14) 1922.
Dienstfertig, A.: Zum chronischen Duodenalulkus im Kindesalter, Deutsche med. Wchnschr. **49:** 1017 (Aug. 3) 1923.
Wright, H. P.: Duodenal Ulcer in Infancy with Report of a Case, Arch. Pediat. **41:** 646 (Sept.) 1924.
Kennedy, R. L. J.: Duodenal Ulcer and Melena Neonatorum, Am. J. Dis. Child. **28:** 694 (Dec.) 1924.
Proctor, O. S.: Chronic Peptic Ulcer in Children, Surg., Gynec. & Obst. **41:** 63 (July) 1925.
Kennedy, R. L. J.: Duodenal Ulcer in Melena Neonatorum: Etiology and Healing Process, Am. J. Dis. Child. **31:** 631 (May) 1926.
Berglund, N.: Zur Kenntnis des Magen- und Duodenalgeschwüres bei Kindern, Acta paediat. **8:** 323, 1929.
Kalk, Heinz: Das Ulcus der Jugendlichen, Ztschr. f. klin. Med. **108:** 225, 1928.
Anderson, K. M.: Perforating Duodenal and Gastric Ulcers in Children, Ugesk. f. læger. **91:** 978, 1929; cited by Hirsch.
de Toni, Giovanni: Sull'ulcera gastro-duodenale nel bambino, Arch. ital. di chir. **26:** 703 (Aug.) 1930.
White, C. S.: Chronic Peptic Ulcer in Childhood, J. Pediat. **3:** 568 (Oct.) 1933.
Muggia: Boll. d. Soc. ital. Pediatr. **2:** 249, 1933; cited by Hirsch.
Bermond, Marco: La diagnosi radiologica dell'ulcera duodenale nell' infanzia, Osservazione personale, Arch. di radiol. **9:** 393 (May-June) 1933; cited by Hirsch.
von Móritz, Dénes: Ein Fall von perforiertem Ulcus duodeni bei einem 2½ jährigen Kinde, Kinderärztl. Praxis **6:** 152 (April) 1935.
Hirsch, Walter: Das Ulcus ventriculi et duodeni beim Kinde, Monatschr. f. Kinderh. **63:** 429 (Nov.) 1935.
Deuticke, Paul: Das chronische Magengeschwür im Kindesalter, Mitt. a. d. Grenzgeb. d. Med. u. Chir. **44:** 290, 1936.
von Lilienfeld-Toal, Marie: Ein Fall von perforiertem Duodenalulcus bei einem 9 jährigen Mädchen, Monatschr. f. Kinderh. **69:** 403, 1937.

burns, nephritis, uremia and infections may lead to secondary ulceration of the gastro-enteric tract. Ulcers due to infection include those associated with tuberculosis, syphilis, typhoid, pneumonia, smallpox, chickenpox, scarlet fever, diphtheria, measles, erysipelas, pemphigus and appendicitis and the like. Duodenal ulceration has been observed repeatedly with tuberculous and other forms of meningitis.[5] Its occurrence in association with meningococcic meningitis, however, was not recorded in the reviews mentioned, although Eckstein[6] stated that hemorrhages sometimes take place in the mucous membranes of the intestine in patients with this disease.

Gerdine and Helmholtz[5] observed diplococci in the base of the ulcer in a large number of children. The organisms were present "in such numbers and in such a position that they presumably are of etiologic significance." In one of their cases there was isolated from the duodenal ulcer Streptococcus viridans, which on injection into rabbits and dogs localized in the pyloric end of the stomach and there produced hemorrhage and ulceration. The authors concluded, with reference to Rosenow's work with the adult, that duodenal ulcer in childhood may be the result of infection with a streptococcus of particular virulence.

Fig. 1.—The duodenal ulcer (× 20).

That a meningococcic infection can also result in the formation of a duodenal ulcer may be suggested by consideration of the following case, which also appears to be of interest in connection with the neurogenic aspects of the pathogenesis of ulcer.[7]

5. Schmidt, W.: Das Ulcus rotundum duodeni im ersten Lebensjahr, Berl. klin. Wchnschr. **50**: 593, 1913. Gerdine, Linton, and Helmholtz, H. F.: Duodenal Ulcer in Infancy: An Infectious Disease, Am. J. Dis. Child. **10**: 397 (Dec.) 1915. Berglund.[4]

6. Eckstein, Albert: Diseases of the Meninges, in Pfaundler, M. V., and Schlossmann, A.: Diseases of Children, Philadelphia, J. B. Lippincott Company, 1935, vol. 5, p. 365.

7. Cushing, Harvey: The Pituitary Body, Hypothalamus and Parasympathetic Nervous System, Springfield, Ill., Charles C. Thomas, Publisher, 1932.

REPORT OF CASE

C. E., a Negro boy, aged 6 years, entered St. Mary's Hospital April 22, 1934, with a temperature of 104.4 F. and a complaint of pain in the chest and the abdomen. That night he had convulsions, and on the following day his neck became rigid. Kernig's sign was elicited. Spinal puncture revealed a pressure of 20 mm. and a cell count of 5,000 per cubic millimeter. No organisms were seen on direct smear.

The next day the patient was transferred to the Contagious Disease Wards of Cincinnati General Hospital, where the following history was obtained: The child had had measles, chickenpox, whooping cough and mumps. He had been vaccinated for smallpox and had received tetanus antitoxin on one occasion. His parents and the two other children of the family, 4 and 8 years of age, were living and well.

On examination the patient, who was rational and cooperative, appeared moderately ill. He complained of a slight pain in his neck. The respirations were not labored, the rate being about 20 a minute. The temperature was 102.2 F., the pulse rate 40 and the blood pressure 85 systolic and 60 diastolic. There was a fading morbilliform rash on the skin of the abdomen, chest and extremities. The pupils were contracted but equal and regular and reacted to light. The pharynx was slightly injected. The lungs were clear to percussion and auscultation. The heart was not enlarged. A loud, blowing systolic murmur was heard over the entire precordium; the rhythm was regular. No masses were felt in the abdomen and no tenderness was elicited. All physiologic reflexes were absent except the abdominal. Kernig's sign was present. A provisional diagnosis of meningococcic meningitis was made.

Spinal puncture, performed April 23, showed a cloudy fluid under a pressure of 18 mm., with 6,000 cells per cubic millimeter, of which 98 per cent were polymorphonuclear leukocytes. Direct smear showed no organisms. The following day the culture of the spinal fluid was positive for meningococci. The patient was given intrathecal injections of antimeningococcus serum, from 15 to 30 cc. daily, receiving a total of 225 cc. over a period of ten days. On several occasions cisternal and spinal punctures were performed simultaneously and irrigation with physiologic solution of sodium chloride was instituted. The patient appeared to be improving. He maintained himself in moderate opisthotonos most of the time. Suddenly, on the morning of May 3, he had slight tremors of his entire body. He was given a sedative and later a soapsuds enema, which was returned with a large amount of soft, slightly formed, brown fecal matter. After this his pulse became irregular and barely perceptible. He died two hours after the onset of the generalized bodily tremors.

Necropsy was performed twelve hours after death. In the examination of the gastro-enteric tract, the esophagus was seen to contain a thick, dark brown fluid, with small particles of undigested food. The stomach was distended with thick, brown, bloody fluid. On the posterior wall of the duodenum, 5 cm. from the pyloric ring, there was a deep, crater-like ulcer with thick, rolled, overhanging edges. This ulcer measured 8 by 12 mm. The surrounding tissues were slightly indurated. The floor of the ulcer was clean and moderately thickened. In the jejunum and the upper half of the ileum thick, sticky, black fecal matter was present. The feces in the colon were slate gray. The Peyer's patches and solitary lymph nodes in both the small intestine and the colon were conspicuous. Those of the ileum, just proximal to the ileocecal junction, were greatly enlarged and congested. No noteworthy changes were observed in the remaining portions of the gastro-enteric tract.

The pancreas was of average size, reddish yellow and quite flabby. Sections through the tail of the pancreas revealed many petechial hemorrhages into the interlobar tissue. In the head of the pancreas these were less conspicuous, although the tissue was congested.

The calvarium and the dura were not remarkable. The vessels over the brain were much congested. There were marked flattening of the cerebral convolutions and narrowing of the fissures. The cerebrospinal fluid was slightly cloudy and had a yellowish tinge. Over the base of the brain there was only a faint yellow clouding along some of the blood vessels. There

was a small amount of subarachnoid hemorrhage around the medulla. The brain weighed 1,215 Gm. Horizontal section at the level of the basal nuclei revealed no pathologic changes other than moderate edema and congestion. The ependyma was thin, smooth and glistening. The venous sinuses were not remarkable. The vessels of the meninges were congested. There was little purulent exudate around the cord. On section its edges rolled outward. No other pathologic changes were noted.

Sections through the duodenal ulcer, stained with hematoxylin and eosin, showed a rather deep, punched-out area disrupting the muscularis mucosae and extending into the longitudinal layer of muscle (fig. 1). The duodenal mucosa was practically intact up to the edges of the ulcer. Some necrotic tissue and a rather extensive amount of fibrinous exudate were present in the floor of the ulcer. There was marked invasion of the tissue surrounding the ulcer by various types of cells, mainly polymorphonuclear leukocytes and lymphocytes, with a few endothelial leukocytes. The area of the pancreas adjacent to the floor of the ulcer showed infiltration of the reacting cells along the fibrous septums of this organ. There was moderate edema

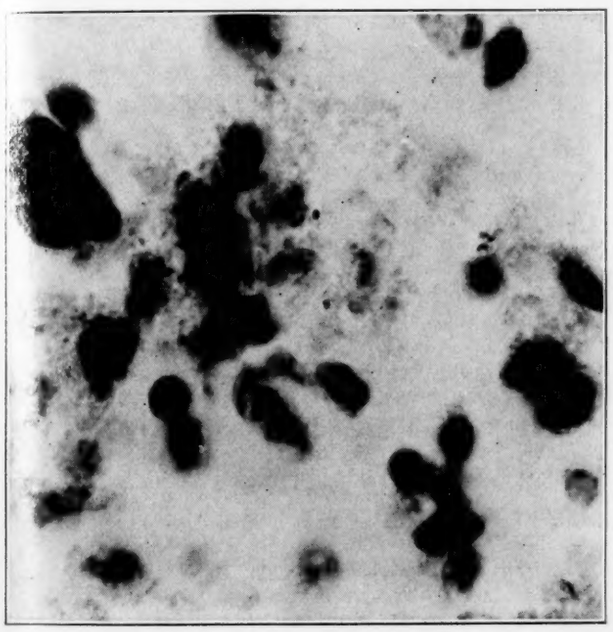


Fig. 2.—Gram-negative diplococci having a structure similar to that of the organisms observed in the meninges (oil immersion lens).

of the tissues surrounding the ulcer. Old eroded blood vessels were seen in the section. Sections stained by the Giemsa and the Gram-Weigert method (fig. 2) showed definite groups of biscuit-shaped, gram-negative diplococci, which had a structure similar to that of the organisms observed in the meninges. Numerous other cocci were found, some arranged in short chains, for the most part gram positive.

The pathologic diagnosis was acute and beginning subacute duodenal ulcer with hemorrhage into the intestine, acute purulent meningitis, severe toxic changes in the viscera, multiple abscesses in the kidneys, acute inflammation of the anterior lobe of the pituitary, multiple focal hemorrhages in the pancreatic tissue with subacute inflammation of the pancreatic ducts, acute ulcerative esophagitis, acute splenitis and generalized lymphadenopathy.

SUMMARY

In a boy, aged 6 years, with meningococcic meningitis, who improved under treatment with antimeningococcus serum, a severe hemorrhage occurred from an ulcer of the duodenum and resulted in death on the twelfth day after the onset of the disease.

Sections of the ulcer showed, among other organisms, groups of biscuit-shaped, gram-negative diplococci having a structure similar to that of the organisms observed in the meninges.

RECURRENT OR RESIDUAL PROGRESSIVE ILEITIS

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In 1932 Ginzburg and Oppenheimer [1] presented their studies of fifty-two cases of nonspecific inflammation of the bowel which had been observed in the previous ten years. An accurate etiologic or pathologic classification of this material was not possible. However, they submitted a classification, "fully conscious of its defects and overlappings but pleading in its favor a certain degree of clinical utility."

One group of fourteen cases presented pathologically a localized chronic nonspecific hypertrophic ulcerative stenosing inflammatory lesion of the terminal ileum, which was sometimes associated with fistula formation. This group, called "regional ileitis," was emphasized in a separate publication with Crohn [2] because of certain typical additional clinical and radiologic features. In the original communication,[1a] illustrative cases were cited. One of the cases of ileitis (case 10) has presented an interesting course since the initial radical operation. Since our knowledge of the ultimate outcome of these patients following various methods of treatment is still limited, a detailed report of this particular case seems warranted and follows herewith:

REPORT OF CASE

History.—H. C.,[3] a man, aged 28, Jewish, clerk, admitted to the hospital Jan. 18, 1928, complained of colicky pains in the abdomen unrelated to meals, of three weeks' duration. On the day of admission the pains became more severe and were referred to the right lower quadrant of the abdomen. There had been no vomiting, diarrhea or chills.

On admission, the temperature was 104, pulse 128. The blood count revealed 20,000 white blood cells with 92 per cent polymorphonuclear leukocytes. There was tenderness, rigidity, and a mass in the right lower quadrant. Clinically the condition was considered an abscess of the appendix. Laparotomy was performed and a large mass was found in the right iliac fossa. The mass was unraveled and found to consist of cecum, appendix, terminal ileum and its mesentery, and a loop of adherent sigmoid. The appendix was lying in a bed in the mesentery of the terminal ileum. It was about 2 inches thick and was oozing pus. The appendix was removed and the area drained. For the first five postoperative days the patient's course was stormy. The temperature was 107.6 F. on the first day and 105.6 for the next two days but finally fell. The patient was discharged on the twenty-first postoperative day with his wound almost completely healed. The pathologic report of the appendix was "acute and chronic inflammation."

Second Admission, May 5 to 19, 1931.—The patient was well for eight months after the appendectomy. Then the scar broke down in one place and drained a purulent, odorless fluid for two months. Spontaneous healing occurred. For the next year and a half the patient had no symptoms. Two weeks before this admission he began to experience pain at the site of his scar, which gradually became more severe. On admission the patient's temperature was 103, and a fluctuant mass presented itself beneath the scar. On incision, about 1 ounce (30 cc.) of thick yellow pus was evacuated. Three days later, fecal drainage was noted. Examination of an injection of iodized oil into the fistula showed that the material entered the cecum and ascending colon. A barium sulfate enema revealed no abnormality of the colon. The patient was discharged with the fecal fistula draining moderately.

Third Admission, July 31 to August 5.—Physical examination was essentially negative except for the presence of an exudate in the right lower quadrant of the abdomen. It was deemed advisable to continue with conservative therapy and the patient was discharged.

Fourth Admission, October 27 to November 22.—The interval history was one of moderate loss in weight, occasional febrile

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1. Ginzburg, Leon, and Oppenheimer, G. D.: (*a*) Nonspecific Granulomata of the Intestine (Inflammatory Tumors and Strictures of the Bowel), Tr. Am. Gastro-Enterol. A., November 1932, pp. 241-273; (*b*) Ann. Surg. **98:** 1046-1062 (Dec.) 1933.

2. Crohn, B. B.; Ginzburg, Leon, and Oppenheimer, G. D.: Regional Ileitis, J. A. M. A. **99:** 1323 (Oct. 15) 1932.

3. This patient was presented with a group of "Cases of Non-Specific Granulomata of the Intestine" before the New York Surgical Society, Nov. 25, 1937, by Dr. Ralph Colp.

episodes and abdominal pains for the past month. There was no diarrhea. An intestinal fistula was still present.

X-ray studies of the sinus following the injection of iodized oil showed that the bulk of the iodized oil entered the cecum and ascending colon. An exploratory laparotomy revealed that the mass which had been palpated previously consisted of greatly thickened indurated edematous terminal ileum. The fistulous tract led to ileum about 4 cm. away from the ileocecal junction. The cecum and ascending colon appeared normal. The ileum was divided 40 cm. proximal to the ileocecal junction and about 10 cm. above the inflamed area. The ileum and 12 cm. of the ascending colon were resected. Both intestinal ends were closed and a side to side, isoperistaltic ileotransverse colonic anastomosis was performed.

The patient made an uneventful convalescence and was discharged feeling well.

Pathologic Examination.—The specimen consisted of 40 cm. of terminal ileum and 12 cm. of ascending colon and attached skin. From the skin a fistulous tract led to a point in the ileum 4 cm. from the ileocecal junction. There were some enlarged,

Six hour plate showing stenotic lesion of ileum up to anastomosis.

moderately firm lymph nodes at the ileocecal angle. Examination of the interior of the specimen showed that the cecum and colon were normal. Beginning at the ileocecal valve and extending upward for 30 cm. there were marked mucosal alterations. The mucosa was congested, thickened and thrown up with irregular folds. The rugae had lost their identity. The surface presented numerous hemorrhages, erosions and ulcerations interspersed with areas of mucosal hyperplasia. The submucous layers were moderately thickened and fibrotic. Above the inflamed area the ileum appeared moderately dilated but otherwise normal.

Microscopic examination revealed marked mucosal ulceration with chronic and acute purulent inflammation, diffuse thickening of all layers of the intestine, especially the submucosa due to edema, granulation tissue and diffuse infiltration with large and small lymphocytes, plasma cells and occasional polymorphonuclear leukocytes. No tubercles or tubercle bacilli were seen.

The pathologic diagnosis was hypertrophic chronic ulcerative inflammation of the ileum.

Follow-Up.—When seen July 3, 1932, the patient felt well; he had gained weight and the bowels moved twice a day. A gastro-intestinal series, taken Nov. 14, 1933, showed no significant changes. The patient was seen on numerous occasions and was well until June 1936, when he began to have watery stools and epigastric pain. June 20 another gastro-intestinal x-ray examination was made. On the four to six hour observations, the distal ileum, for a distance of 10 inches proximal to the stoma, appeared to be the site of a marked ulcerative, stenosing lesion, as shown in the accompanying illustration.

Fifth Admission, Nov. 5-26, 1936.—The interval history, five years after resection, was one of occasional attacks of diffuse abdominal pain with three watery bowel movements a day but without pus or blood. The physical examination was essentially negative. The blood Wassermann reaction and urinalysis were negative.

Operation was performed November 7 under spinal anesthesia. The terminal 18 inches of ileum showed the characteristic lesion of ileitis. Its peritoneal surface was dull, the wall was thickened, inflamed and edematous. Large lymph nodes were present in the mesentery. The ileum was divided proximal to the inflamed area. Both ends were closed and an ileosigmoidal side to side isoperistaltic anastomosis was performed with the upper loop.

Postoperative Course and Follow-Up.—The patient made an uneventful recovery and was discharged feeling well. He visited the Follow-Up Clinic Jan. 21, 1937, and was found to have gained 7 pounds (3.2 Kg.). He was well and asymptomatic. August 4 the patient was working, was feeling well and was having several soft bowel movements daily.

COMMENT

Obviously there are two possibilities to explain the presence of disease after a primary resection. Either it is a true recurrence of a previously uninvolved ileum or the disease was present and unrecognized, following which it persisted and progressed to cause symptoms. Another comparable case has come to my attention from this hospital.[3a] Jackson [4] in a recent paper describes a similar case in a woman. His presentation gives perhaps the life history of the disease. When first seen in 1909 the patient was operated on because of pain in the right lower quadrant, vomiting and diarrhea. The preoperative diagnosis was appendicitis but the lesion appeared to be what is now recognized as an ileitis. Nothing but an appendectomy was performed. From then on she had recurrent attacks of abdominal cramps with free intervals. She was operated on in May 1929 (twenty years later) and the lower part of the ileum and the cecum were removed. The lesion was pathologically an ileitis. The patient was free from attacks until five years later, when in 1934 severe cramplike pains recurred. A gastro-intestinal series showed a lesion in the distal 30 cm. of ileum up to the anastomosis. A third operation (ileocolic resection) was performed in 1935, and the lesion of a recurrent or residual ileitis similar to the original lesion was found. The disease involved only the small intestine, stopping sharply at the anastomosis. Shearer and Jackson [5] reported a case of ileitis with twice recurrent disease after apparently wide resections.

From these observations it does not seem possible to differentiate between a residual and a recurrent lesion. Even if radical operation had completely removed the disease, it is not illogical to suppose that the etiologic factors (which are still unknown) may have persisted and caused the subsequent involvement of the new terminal ileum. On the other hand, in favor of a persistent residual lesion with subsequent progression is the possibility that the early lesion of the disease is so minimal that what was considered normal ileum may have already been involved but not evident to the eye or touch.

It might be advisable, when doing either a radical excision or the conservative division of ileum with ileocolonic anastomosis, to divide the ileum at least 8 to 12 inches proximal to visible or palpable involvement. In addition, the operator should examine the ileum carefully far above the lesion, looking for inflammation, since it is known now that "skip" or inflamed areas may occur between which lie portions of normal ileum.

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3a. Since this report was submitted for publication a third patient, a personal one, has returned with vague abdominal cramps and diarrhea. X-ray studies suggest a stenosing lesion of the terminal ileum. The patient was a man, aged 29, who was operated on three years ago in this hospital. A wide ileocecal resection was performed for a typical regional ileitis without fistula. As yet, a secondary operation has not been done.

4. Jackson, A. S.: Regional Enteritis, Surg., Gynec. & Obst. **65:** 1-10 (July) 1937.

5. Shearer, J. P., and Jackson, J. T.: Recurrent Regional (Terminal) Ileitis, Ann. Surg. **106:** 459-461 (Sept.) 1937.

Special Article

CHEMICAL ASPECTS OF RIBOFLAVIN

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WASHINGTON, D. C.

This article and others recently published or to be published comprise a new series on the present status of our knowledge of the vitamins. They have been prepared under the general auspices of the Council on Pharmacy and Chemistry and the Council on Foods. The opinions expressed are those of the authors and not necessarily the opinions of either council. The articles will be published later in book form.—ED.

HISTORICAL SKETCH

The chemical nature of the water-soluble yellow green-fluorescent pigment of whey now referred to as riboflavin (synonymous with lactoflavin, vitamin G and vitamin B_2, as used by many English and German investigators) commanded the attention of chemists [1] as early as 1879. A considerable concentration of this pigment was effected and certain of its more obvious chemical properties were clearly set forth by Bleyer and Kallmann [2] in 1925. No unusual significance was associated with this pigment by these early workers, who apparently regarded it only as one of the minor constituents of milk, the chemical nature of which was quite obscure.

In 1932 Warburg and Christian [3] described a new oxidation enzyme obtained from aqueous extracts of yeast. The enzyme in water solutions was yellow and exhibited a green fluorescence. Together with a second enzyme obtained from yeast and a co-enzyme obtained from the red blood cells of horse blood this "yellow enzyme" constituted an enzyme system capable of oxidizing Robison's hexose-monophosphoric acid ester. The "yellow enzyme" was reversibly reduced to its leukoform during the process. To regenerate the pigmented enzyme it was necessary only to shake the solution carrying it in leukoform with molecular oxygen. In this system the "yellow enzyme," by virtue of its easily reversible oxidation-reduction reactions, acts as an oxygen transport between molecular oxygen and the substrate. It has now been practically established that this "yellow enzyme" is present in every living cell or at least in the cells of all the higher forms of life.[4]

Warburg and Christian [5] were able to separate the "yellow enzyme" from yeast and to split it into a protein component and a pigment component. Neither component alone was catalytically active. The separation of these components was effected by addition of three volumes of methyl alcohol to a water solution of the enzyme at a temperature of 38 C., whereupon the protein was denatured, leaving the pigment component in solution. These brilliant researches constitute the first separation and identification of the prosthetic or chemically active grouping of an enzyme. Irradiation of alkaline solutions of the pigment component followed by acidification of the irradiated solution yielded a yellow chloroform soluble photoderivative (later designated lumiflavin). Studies of the chemical nature of this photoderivative, which can also be obtained readily from the relatively heat-stable vitamin riboflavin, constituted the crux in the elucidation of the chemical structure of the vitamin and of the prosthetic group of the enzyme.

In 1933 there appeared almost simultaneously from three different laboratories reports supporting a relationship and probable identity of the water-soluble yellow green-fluorescent pigments widely distributed in animal and plant products with vitamin G or vitamin B_2, the accepted chemical name for which is now riboflavin. Ellinger and Koschara [6] called attention to the presence of a group of water-soluble yellow green-fluorescent pigments present in milk, liver, kidneys, urine, muscle, yeast and plant materials for which they suggested the name lyochromes, in contradistinction to the group of naturally occurring fat-soluble pigments, lypochromes. These authors suggested also the probable relationship of these pigments to the yellow enzyme discovered by Warburg and Christian. Any one thoroughly familiar with the properties and distribution of the vitamin riboflavin could readily discern from their report the similarity of the qualities of the vitamin with the attributes of the pigments designated as lyochromes.

About the same time I [7] had succeeded in obtaining from whey powder several concentrated growth-promoting supplements for the Bourquin-Sherman [8] vitamin G-deficient diet, the vitamin potencies of which paralleled the intensities of yellow pigmentation.

Kuhn and his co-workers [9] had isolated a water-soluble yellow green-fluorescent pigment from dried egg albumin and reported [10] that the crystalline product was a growth-promoting supplement for the Bourquin-Sherman diet, 100 micrograms a day inducing a growth rate in rats of about 10 Gm. a week. In subsequent studies these workers seemingly had difficulty with the Bourquin-Sherman diet and found it necessary to supplement it further with concentrates of unidentified factors present in yeast extracts. These authors also called attention to the similarity in distribution of the vitamin and the water-soluble yellow pigments and to their probable relationship with the yellow enzyme. They suggested the chemical group name of flavins for these pigments, the ending "-in" denoting that they contained nitrogen as an elemental constituent. Since there appeared to be differences in the relative vitamin activities of the yellow pigment preparations, they assumed that there were inherent differences in chemical nature associated with variation in source materials. Pending further chemical investigations they proposed to differentiate them by appropriate prefixes such as ovo-, lacto- and hepato-flavins.

Further investigation has shown that an identical flavin having a d-ribose residue attached to the tricyclic chromophore nucleus (characteristic of all flavins) is

From the Bureau of Home Economics, U. S. Department of Agriculture.

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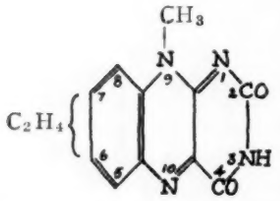
2. Bleyer, B., and Kallmann, O.: Beiträge zur Kenntnis einiger bisher wenig studierter Inhaltsstoffe der Milch (Kuhmilch) II, Biochem. Ztschr. **155**: 54-79 (Jan.) 1925.
3. Warburg, Otto, and Christian, Walter: Ueber ein neues Oxydationsferment und sein Absorptionsspektrum, Biochem. Ztschr. **254**: 438-458 (Oct.) 1932.
4. Warburg, Otto, and Christian, Walter: Ueber das Gelbe Ferment und seine Wirkungen, Biochem. Ztschr. **266**: 377-411 (Nov.) 1933.
5. Warburg, Otto, and Christian, Walter: Ueber das neue Oxydationsferment, Naturwissensch. **20**: 980-981 (Dec. 16/23) 1932.
6. Ellinger, Philipp, and Koschara, Walter: Ueber eine neue Gruppe tierischer Farbstoffe (Lyochrome), Ber. d. Deutschen chem. Gesellsch. **66**: 315-317 (Feb.) 1933; Ueber eine neue Gruppe tierischer Farbstoffe (Lyochrome), ibid. **66**: 808-813 (June) 1933
7. Booher, Lela E.: The Concentration and Probable Chemical Nature of Vitamin G, J. Biol. Chem. **102**: 39-46 (Sept.) 1933.
8. Bourquin, Anne, and Sherman, H. C.: Quantitative Determination of Vitamin G (B_2), J. Am. Chem. Soc. **53**: 3501-3505 (Sept.) 1931.
9. Kuhn, Richard; György, Paul, and Wagner-Jauregg, Theodor: Ueber Ovoflavin, den Farbstoff des Eiklars, Ber. d. Deutschen chem. Gesellsch. **66**: 576-580 (April) 1933.
10. Kuhn, Richard; György, Paul, and Wagner-Jauregg, Theodor: Ueber eine neue Klasse von Naturfarbstoffen (Vorläufige Mitteilung), Ber. d. Deutschen chem. Gesellsch. **66**: 317-320 (Feb.) 1933.

obtained from a variety of natural source materials. Other flavins and flavin derivatives have been synthesized with various groups replacing the d-ribose residue and some of these possess vitamin activity. However, none of these now known possess greater vitamin potency than d-riboflavin and probably all of them are less potent than riboflavin.

The use of the term d-riboflavin or just riboflavin as a substitute for the terms vitamin B_2 or vitamin G was suggested [11] by the Council on Pharmacy and Chemistry. This terminology was later approved by the Committee on Vitamin Standards, American Society of Biological Chemists, and also by the Committee on Vitamin Nomenclature, American Institute of Nutrition (April 1937).



I. Lumiflavin—a predicted partial structural formula.

The remainder of the story of the chemistry of riboflavin is the story of the elucidation of the intimate structure of the molecule, its characteristic properties, its many derivatives and its relation to the "yellow oxidation enzyme."

ISOLATION

Riboflavin has been isolated from a wide variety of animal and plant products, including egg white,[9] milk,[12] liver,[13] kidney,[14] urine,[15] barley malt,[16] dandelion blossoms,[17] grasses,[18] egg yolk [19] and retinas of fish eyes.[20] It cannot be stated with absolute certainty that the crystalline flavin obtained from each of these various sources is chemically identical with riboflavin, but such is the case at least for those to which adequate determinative tests have been applied. Four synthetic flavins closely related chemically to riboflavin have been reported [21] to possess vitamin activity, but so far none of these have been reported to occur in natural products.

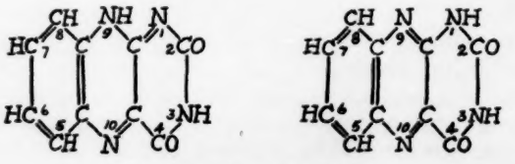
The isolation of riboflavin from these many naturally occurring source materials has been accomplished through the independent efforts of several laboratories. The several methods of isolation employed, although slightly diversified in certain detailed manipulations, have much in common. The successive steps in the isolation procedures may be summarized in a general way as follows: (1) extraction of flavin-containing material with aqueous acid solutions, with alcohol or with water-alcohol mixtures; (2) adsorption of the flavin from the extract on fullers' earth, lead sulfide or other suitable adsorbent usually from acid solution; (3) elution of the flavin from the adsorbent by means of pyridine, pyridine-methyl alcohol-water mixtures, or ammonia in water or in water-alcohol mixtures; (4) removal of elution solvent with recovery and concentration of the flavin in water or alcohol solution followed by elimination of acetone insoluble impurities; (5) precipitation and crystallization of a heavy metal (notably silver or thallium) salt of the flavin which is soluble with difficulty and easily crystallized, and (6) recovery of the metal-free flavin followed by repeated crystallizations from water, alcohol or dilute acetic acid solutions.

In their earlier work, Kuhn and his co-workers [9] obtained from 100 Kg. of dried egg albumin, corresponding to about 33,000 eggs, 100 mg. of thrice recrystallized flavins. According to subsequent measurements [22] of the quantities of flavin normally present in dried egg albumin, this yield would correspond to around 7 per cent of the total flavin present in the egg albumin. Similarly the yield of crystalline flavin from milk as reported [23] in the earlier work was not greater than 5 per cent of the total quantity present. The use of heavy metal precipitations increased the yield to around 18 to 20 per cent of the quantity reported [22] to be normally present in milk.

Riboflavin crystallizes from absolute alcohol as yellow-orange, needle shaped crystal clusters. The crystals possess no sharp melting point but rather begin to darken at about 240 C. and decompose at temperatures of around 274 to 282 C. The tetraacetyl derivative liquefies with decomposition at about 238 to 242 C. Elementary analysis of the riboflavin crystals established the empirical formula $C_{17}H_{20}N_4O_6$ corresponding to a molecular weight of 376.

ELUCIDATION OF RIBOFLAVIN STRUCTURE

Following the isolation of riboflavin in crystalline form, the next step directed toward ultimate synthesis of the compound rested on elucidation of its characteristic chemical features. Warburg and Christian [4] had already isolated a photoderivative from the pigment component of their yellow enzyme and had expounded many of its more salient properties. Exposure of alkaline solutions of the pigment component to ultraviolet irradiation or ordinary light resulted in the formation of a yellow photoderivative (lumiflavin), soluble with difficulty in water but soluble in chloroform and



II. Iso-alloxazine and alloxazine.

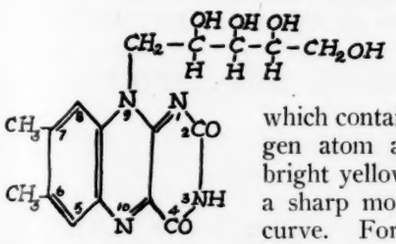
having the empirical formula $C_{13}H_{12}N_4O_2$. The course of this reaction could be followed by acidifying a portion of the solution at intervals and extracting the solution with chloroform. This photoderivative exhibited spectral properties very similar to those of the pigment component of the enzyme having two characteristic absorption bands in the ultraviolet region and one in the visible wavelength range. The yellow color of the photoderivative could be reversibly dispelled by reduction with hydrogen in the presence of palladium. Warming a solution of the photoderivative in the

11. Council on Pharmacy and Chemistry: Riboflavin, the Accepted Name for Vitamin B_2, J. A. M. A. **108:** 1340-1341 (April 17) 1937.
12. Kuhn, Richard; Rudy, Hermann, and Wagner-Jauregg, Theodor: Ueber Lactoflavin (Vitamin B_2) Ber. d. Deutschen chem. Gesellsch. **66:** 1950-1956 (Dec.) 1933.
13. Karrer, Paul; Salomon, H., and Schöpp, K.: Isolierung des Hepaflavins, Helvet. chim. acta **17:** 419-425 (March) 1934.
14. Karrer, Paul: Ueber einige natürlich vorkommende, biochemisch bemerkenswerte Pigmente, Helvet. chim. acta **19:** E 33-E 48 (Aug.) 1936.
15. Koschara, Walter: Ueber ein Lyochrom aus Harn (Uro-flavin), Ber. d. Deutschen chem. Gesellsch. **67:** 761-766 (May) 1934. Karrer.[14]
16. Karrer, Paul, and Schöpp, K.: Isolierung des Flavins aus Malz, Helvet. chim. acta **17:** 1013-1014 (Nov.) 1934.
17. Karrer, Paul, and Schöpp, K.: Isolierung eines pflanzlichen Flavins, Helvet. chim. acta **17:** 771-772 (July) 1934.
18. Kuhn, Richard, and Kaltschmitt, Hans: Isolierung von Lactoflavin (Vitamin B_2) aus Heu, Ber. d. Deutschen chem. Gesellsch. **68:** 128-131 (Jan.) 1935.
19. Karrer, Paul, and Schöpp, K.: Isolierung des Lyochroms aus Eigelb (ovoflavin G), Helvet. chim. acta **17:** 735-737 (July) 1934.
20. Euler, Hans, and Adler, Erich: Ueber das Vorkommen von Flavinen in tierischen Geweben, Ztschr. f. physiol. Chem. **223:** 105-112 (Feb.) 1934.
21. Karrer, Paul, and Quibell, T. H.: Synthesen einiger neuer Flavine, Helvet. chim. acta **19:** 1034-1042 (Oct.) 1936.
22. Kuhn, Richard; Wagner-Jauregg, Theodor, and Kaltschmitt, Hans: Ueber die Verbreitung der Flavine im Pflanzenreich, Ber. d. Deutschen chem. Gesellsch. **67:** 1452-1457 (Aug.) 1934.
23. Kuhn, Richard; György, Paul, and Wagner-Jauregg, Theodor: Ueber Lactoflavin, den Farbstoff der Molke, Ber. d. Deutschen chem. Gesellsch. **66:** 1034-1039 (July) 1933.

presence of barium hydroxide liberated urea,[4] thereby disclosing its alkali lability and paving the way for the later disclosure of the presence of an -NH-CO-NH- grouping.

The suggestion of a probable relationship of the yellow enzyme and the vitamin riboflavin stimulated no inconsiderable interest in this photoderivative. It was soon found [12] that irradiation of alkaline solutions of riboflavin resulted in the splitting off of a hydroxyl-rich side chain, the latter being responsible for the solubility of the vitamin in water. Since the elementary composition of both the vitamin ($C_{17}H_{20}N_4O_6$) and that of the photoderivative ($C_{13}H_{12}N_4O_2$) had been ascertained, the portion split off must correspond to $C_4H_8O_4$ ($C_{17}H_{20}N_4O_6 - C_{13}N_{12}N_4O_4 = C_4H_8O_4$). Furthermore, acetylation of riboflavin yielded a tetra-acetyl derivative associated with the 4- carbon portion split off by photolysis. One primary alcohol group in the hydroxyl-containing side chain was established from quantitative measurements of the formaldehyde formation resulting from the application of suitable oxidation procedures. The group split off then by photolysis must necessarily correspond to a side chain of the structure -CHOH.CHOH.CHOH.CH_2OH.

Kuhn and Rudy [24] made further intensive studies of the products of alkaline hydrolysis of riboflavin and lumiflavin. By heating alkaline solutions of either riboflavin or lumiflavin they obtained urea and an organic acid, $C_{12}H_{12}N_2O_3$, which contained one active hydrogen atom and which formed a bright yellow silver salt and gave a sharp monobasic acid titration curve. For the splitting off of urea by alkaline hydrolysis of lumiflavin, two molecules of water were required. This would indicate that the urea-yielding group belonged to a ring system and not to a side-chain ureide or guanidino group wherein only one molecule of water would be required. These observations, jointly considered, make it evident that both oxygen atoms of lumiflavin ($C_{13}H_{12}N_4O_2$) belong to an alkalilabile ring, one going to form urea and the other to build the carboxyl group in the organic acid $C_{12}H_{12}H_2O_3$.



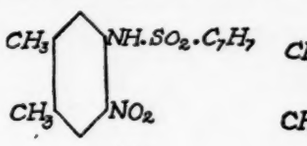
III. d-riboflavin.

Further studies [25] led to the finding that both lumiflavin and the organic acid $C_{12}H_{12}N_2O_3$ contained an alkylimide grouping, in contrast to riboflavin, in which this grouping is absent. Apparently then the sugar-like side-chain split off by photolysis of riboflavin was replaced by an alkyl group. As a result of the studies of the decomposition products of riboflavin and lumiflavin the partial structural formula I for the latter was advanced by Kuhn.

In the riboflavin molecule a d-ribityl group replaces the methyl group of lumiflavin at position 9. This proposed structure definitely related riboflavin and lumiflavin to the alloxazine series of organic compounds, which were first discovered by Kühling [26] in 1891 and which possessed many properties similar to those of flavins.

The structures of alloxazine and its tautomeric form, iso-alloxazine, are represented in formula II.

Riboflavin and lumiflavin are derivatives of iso-alloxazine, since riboflavin and lumiflavin each possess only one active hydrogen atom, namely at position 3, while the alloxazine molecule contains two active hydrogen atoms (positions 1 and 3). In riboflavin and lumiflavin the hydrogen attached to the nitrogen at position 9 is replaced by a pentose residue and a methyl group, respectively.



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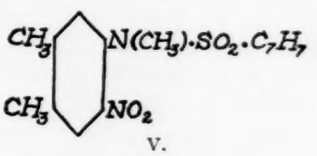


V.

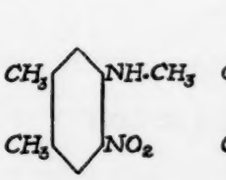
A structural formula III was predicted for riboflavin and subsequently confirmed by synthesis. The formula shows the side-chain as ribose.

It was not known in the early stages of the investigations, of course, that the spacial relationships of the hydroxyl-containing side-chain corresponded specifically to d-ribose.

SYNTHESIS OF LUMIFLAVIN AND RIBOFLAVIN

Once the essential structural features of riboflavin had been deciphered, attempts to synthesize many of its chemically related compounds were quick to follow. The synthesis of lumiflavin was achieved before that of the vitamin. Except for the reaction involving condensation of the 6,7-dimethyl derivative of ortho-phenylenediamine with alloxan, a reaction based on the earlier work of Kühling [26] and Kühling and Kaselitz,[27] the steps involved in the synthesis of this compound are well known in the field of organic chemistry.

The synthesis of lumiflavin as developed by Kuhn and his co-workers [27a] is as follows: Ortho-xylene on treatment with nitric acid yields 1,2-dimethyl-4,5-dinitrobenzene, which on partial reduction yields 1,2-dimethyl-4-nitro-5-aminobenzene. The latter is heated at 100 C. with paratoluene sulfone chloride in pyridine for four to five hours and yields a product with formula IV. This intermediate on treatment with dimethyl sulfate and alkali at 50 to 60 C. yields a methyl derivative V. Hydrolysis of this derivative can be accomplished with a mixture of glacial acetic and concentrated sulfuric acids and there is produced the methyl amino compound VI. The nitro group of compound VI is reduced with stannous chloride and hydrochloric acid to yield the amino compound VII. The hydrochloride of compound VII is condensed with a slight excess of alloxan VIII in water at 50 to 60 C. to yield lumiflavin IX; the yield over all is about 75 per cent.



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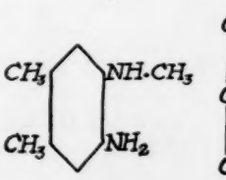

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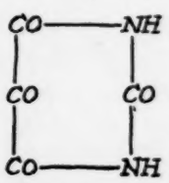


VIII.

24. Kuhn, Richard, and Rudy, Hermann: Ueber den alkali-labilen Ring des Lacto-flavins, Ber. d. Deutschen chem. Gesellsch. **67**: 892-898 (May) 1934.

25. Kuhn, Richard, and Rudy, Hermann: Ueber die Konstitution des Lumilactoflavins, Ber. d. Deutschen chem. Gesellsch. **67**: 1298-1299 (July) 1934.

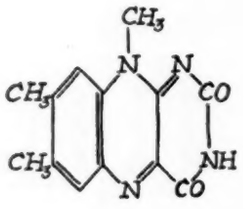
26. Kühling, O.: Ueber azine der Harnsäuregruppe, Ber. d. Deutschen chem. Gesellsch. **24**: 2363-2369 (July) 1891.

27. Kühling, O., and Kaselitz, O.: Ueber Condensationsproducte N-substituirter O-Diamine mit Alloxan und dessen Derivaten, Ber. d. Deutschen chem. Gesellsch. **39**: 1314-1326 (March) 1906.

27a. Kuhn, Richard, and Reinemund, Karl: Ueber die Synthese des 6, 7, 9, Trimethyl-flavins (Lumi-lactoflavins) Ber. d. Deutschen chem. Gesellsch. **67**: 1932-1936 (Nov.) 1934.

The alkaline hydrolysis of lumiflavin forms urea and an alkaline salt of the organic acid $C_{12}H_{12}N_2O_3$, X, a reaction of material assistance in elucidating the structure of the tricyclic chromophore nucleus of riboflavin.

Without the presence of the modified pentose side-chain attached to the N-atom position 9 (see proposed structural formula III for riboflavin) the flavin possesses no vitamin activity. Since the grouping -CHOH.-CHOH.CHOH.CH_2OH possesses three asymmetrical



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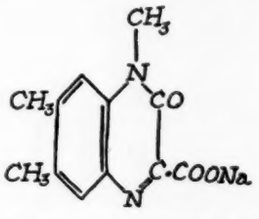
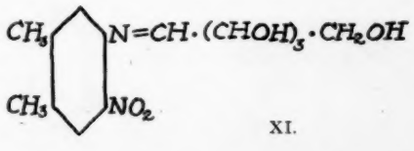


X. Salt of the acid $C_{12}H_{12}N_2O_3$.

carbon atoms, there existed eight theoretically possible stereoisomers of the proposed structure, one of which presumably would be identical to that in natural riboflavin. The possibility was also tenable that more than one configuration would exhibit vitamin activity. The selection of possibilities which might yield a product identical with the naturally occurring vitamin could be somewhat narrowed in view of the optical activity of the vitamin as isolated. The vitamin exhibited optical activity only in alkaline solution, in which case it was levorotatory, and presumably the relative spacial relations of the -H and -OH groups nearest the chromophore group of the vitamin control the sign of rotation. This information narrowed the choice to l-arabinose, d-xylose and d-ribose residues for the hydroxyl-containing side-chain which might be identical with that in the vitamin molecule. The pentyl side-chain corresponding to d-ribose was finally proved to have the same spacial relationships as the side-chain involved in the naturally occurring vitamin. The synthetic d-riboflavin was identical in chemical properties with the vitamin as isolated from various source materials and the mixed melting point (attended with decomposition) of the synthetic and natural products indicated no depression of this constant.

The synthesis of d-riboflavin as developed by Kuhn and his co-workers [28] was the same as that for lumi-



XI.

flavin to the stage of formation of 1,2-dimethyl-4-nitro-5 amino-benzene. This compound on heating with d-ribose yields compound XI. The latter can be reduced with platinum black to give XII. On treatment with alloxan in a mixture of acetic and boric acids, a condensation occurs with the formation of d-riboflavin III.

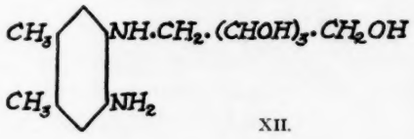
Karrer and his co-workers [29] meanwhile had also developed a method of synthesis for d-riboflavin and recently [30] have described an improved method giving a yield of about 38 per cent of the theoretical yield calculated on the basis of the quantity of d-ribose employed. Starting with 2 Gm. of d-ribose they obtained approximately 2 Gm. of riboflavin.

The chief obstacle involved in the preparation of the synthetic vitamin riboflavin is the limited availability of the essential d-ribose. The supply of d-ribose used by both Karrer [30] and Kuhn [28] was prepared from d-arabinose, which in turn was obtained from the calcium salt of d-gluconic acid, a synthesis of five steps summarily attended with considerable losses. Kuhn and his co-workers [28] report that from 2 Kg. of the calcium salt of d-gluconic acid (yielding about 500 Gm. of d-arabinose) they obtained 53 Gm. of d-ribose.

The l-araboflavin has been synthesized [31] and found to possess vitamin activity, but in comparison to d-riboflavin it has been reported [32] to be only about one third as potent.

PROPERTIES OF RIBOFLAVIN AND RELATED COMPOUNDS

Syntheses of many derivatives of riboflavin have demonstrated the extremely limited alterations of the structural configuration of the riboflavin molecule compatible with vitamin activity. While the tricyclic chromophore nucleus is common to all flavins, the position and kind of substituent groups on the benzene ring and the nature of the side-chain attached to



XII.

the nitrogen atom in position 9 are determinate factors for vitamin activity. The following synthetic flavins have been shown to possess vitamin activity: 6,7-dimethyl-9-[d,l'ribityl]-iso-alloxazine (riboflavin),[33] 6,7-dimethyl-9-[1,l'arabityl]-iso-alloxazine (araboflavin),[31a] 7-monomethyl-9-[d,l'ribityl]-iso-alloxazine,[21] 6-monomethyl-9-[d,l'ribityl]-iso-alloxazine [21] and 6 ethyl-7 methyl-9-[d,l'ribityl]-iso-alloxazine.[21]

At least one of the methyl groups in position 6 or 7 is essential in order that the flavin molecule shall possess vitamin activity. The absence of both the 6 and 7 methyl groups actually appears to be accompanied with toxicity.[34] As regards the side-chain, only d-ribose or d-arabinose residues attached to the nitrogen atom in position 9 have thus far proved to be compatible with vitamin activity of the flavins. Exceedingly small variations in this side-chain are attended with complete lack of vitamin activity.

Fluorescence.—One of the most characteristic properties of riboflavin is its yellow green-fluorescence in neutral solutions. The fluorescence is at a maximum in the region of p_H 6.0 to p_H 7.0 and decreases in either more acid or more alkaline solutions. This observation would indicate that riboflavin was ampho-

28. Kuhn, Richard; Reinemund, Karl; Weygand, Friedrich, and Ströbele, Rudolf: Ueber die Synthese des Lactoflavins (Vitamin B_2), Ber. d. Deutschen chem. Gesellsch. **68**: 1765-1774 (Sept.) 1935.

29. Karrer, Paul; Becker, B.; Benz, F.; Frei, P.; Salomon, H., and Schöpp, K.: Zur Synthese des Lactoflavins, Helvet. chim. acta **18**: 1435-1448 (Oct.) 1935.

30. Karrer, Paul, and Meerwein, H. F.: Eine verbesserte Synthese des Lactoflavins und 6, 7-dimethyl-9-[l'-arabityl]-iso-alloxazins, Helvet. chim. acta **19**: 264-269 (March) 1936.

31. (*a*) Kuhn, Richard, and Weygand, Friedrich: Synthetisches Vitamin B_2, Ber. d. Deutschen chem. Gesellsch. **67**: 2084-2085 (Dec.) 1934. (*b*) Karrer, Paul; Schöpp, K.; Benz, F., and Pfaehler, K.: Synthesen von Flavinen III, Helvet. chim. acta **18**: 69-79 (Dec.) 1935.

32. Kuhn, Richard; Rudy, Hermann, and Weygand, Friedrich: Ueber die Zuckerähnliche Seitenkette des Lactoflavins, Ber. d. Deutschen chem. Gesellsch. **68**: 625-634 (April) 1935.

33. Kuhn, Reinemund, Weygand and Ströbele.[28] Karrer and Meerwein.[30]

34. Kuhn, Richard, and Boulanger, Paul: Ueber die Giftigheit der Flavine, Ztschr. f. physiol. Chem. **241**: 233-238 (July) 1936.

teric in nature and that the electrically neutral molecule was responsible for the fluorescence. Kuhn and Moruzzi [35] made a series of fluorescence measurements of riboflavin solutions with graded p_H values. At p_H 1.7, on the acid side, and at p_H 10.2, on the alkaline side, the fluorescence was 50 per cent of its maximum value. Using these data in the generally accepted manner for calculation of the dissociation constants of base, acid and iso-electric point they obtained the following values:

$$k_{acid} = 63 \times 10^{-12},\ k_{base} = 0.5 \times 10^{-12} \text{ and iso-electric point, } p_H\ 6.0.$$

These authors used ultraviolet rays and were of the opinion that in the region of optimum p_H the fluorescence brightness was proportional to the riboflavin concentration.

Later, Karrer and his co-workers [36] reported that maximum fluorescence of solutions (p_H 7.0) of riboflavin appeared with concentrations of 0.003 per cent, the fluorescence intensity decreasing with either greater or lesser concentrations. They suggest that Kuhn and his co-workers probably used such dilute flavin solutions that the measurements were all made far below the maximum fluorescence brightness.

The fluorescence measurements for lumiflavin gave practically the same k_{acid} and k_{base} constants as those for riboflavin, indicating that the sugar-like side-chain of riboflavin has very little influence on the electrolytic properties of the molecule.[35]

The retinas of the eyes of many species of animals have been reported [20] to contain relatively high concentrations of flavin, the concentration corresponding rather closely to that at which maximum fluorescence occurs. It is supposed that the flavins are involved in some balanced light sensitized reactions concerned with dim vision.

Optical Activity.—In neutral solutions or in acid solutions wherein the riboflavin exists as a positively charged ion, the optical activity of riboflavin is exceedingly small. In nonfluorescent alkaline solutions of riboflavin the maximum rotation (levo-) was observed[37] when one mole of riboflavin is in the presence of one mole of sodium hydroxide. This maximum rotation was given as $[a]_D^{20} = \frac{-0.51° \times 100}{0.447 \times 1} = -114°$ (in 0.1 N NaOH). Karrer and Fritzsche [38] confirm this dependence of specific rotation on the relative concentrations of riboflavin and alkali.

Solubility and Stability.—Riboflavin, owing to the presence of its d-ribityl side-chain, is a typically water-soluble type of compound and is insoluble in the ordinary fat solvents. By splitting off this d-ribityl side-chain the resultant molecule becomes soluble in such solvents as chloroform.

Riboflavin is quite stable in strong mineral acids but sensitive to alkali. Riboflavin is sensitive to light and on irradiation with ultraviolet rays or visible light undergoes irreversible decomposition. Irradiation of alkaline solutions is attended with the formation of lumiflavin, $C_{13}H_{12}N_4O_2$. Irradiation of neutral or acid solutions of riboflavin is attended with the formation of 6,7-dimethyl-alloxazine, or "lumichrome," [39] which exhibits an intense blue fluorescence.

Riboflavin is quite stable to oxidizing agents, including hydrogen peroxide, bromine water and concentrated nitric acid. It is oxidized by chromic acid, yielding ammonia, carbon dioxide and a nitrogen-free residue.

Riboflavin is reversibly reduced by hydrogen (palladium or platinum and hydrogen, zinc in presence of acid), by sodium thiosulfate and by hydrogen sulfide in alkaline solution and by titanous chloride.

Oxidation-Reduction Potential—The very unique as well as complicated oxidation-reduction systems of the flavins have attracted unusual attention and also have caused a considerable volume of literature to be built up.

The flavins represent very stable oxidation-reduction systems, imparting quite reproducible potentials to noble metal electrodes within a reasonable range of buffering capacity. In relation to molecular structure it has been shown [40] that acetylation, methylation or loss of the sugar-like side-chain of riboflavin does not materially affect the oxidation-reduction potential of the flavin. Titration of the completely reduced flavin with a suitable oxidant (or vice versa) at graded p_H values forms the basis for a series of curves which have been variously reported as corresponding to a one electron system and a two electron system and an intermediate electron system. Apparently the electron number shifts and is different at different ranges of p_H values, which would account for some of the divergence in reports. According to Stern,[41] the slope of the titration curves in the range of p_H 6.0 to 12.4 corresponds to that of a two electron system. From p_H 4.0 to p_H 1.0 the character of the curves is that of a one electron system, while at p_H values of less than one the steepness of the curves gradually increases until at p_H 0.4 two maxima appear, indicating a two-stage process. At p_H values less than 5.0 a red intermediate compound, as first noted by Kuhn and his co-workers,[42] appears, which becomes more pronounced as the two-stage separation is approached at about p_H 0.4.

The normal potential of riboflavin referred to the normal hydrogen electrode is in the region of —0.21V (p_H 7.0) as reported by many investigators, including those referred to. The physiologic significance of the extremely negative position of the normal potentials of the flavins is not at present understood. Under the general anaerobic reduction potential of living cells, the cell flavin is said [43] to be exactly in its equilibrium range.

In a recent report, Kuhn and Ströbele [44] state that in the conversion of riboflavin to leuko-riboflavin no less than three different reduction intermediates intervene and that these are distinguishable by vivid colors and sharp definite compositions.

Absorption of Light by Flavins.—Riboflavin, lumiflavin and the yellow enzyme exhibit characteristic absorption bands with well defined maxima in approx-

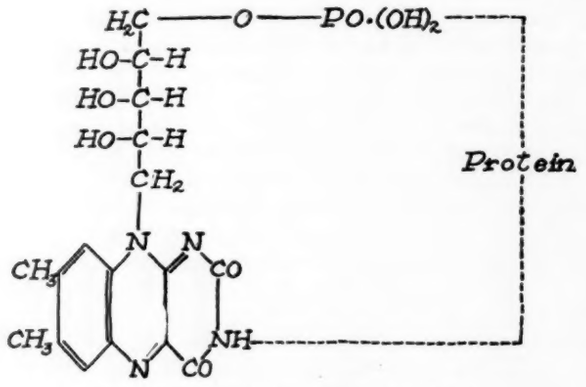
35. Kuhn, Richard, and Moruzzi, Giovanni: Ueber die Dissoziationskonstanten der Flavine; p_H-Abhängigkeit der Fluorescenz, Ber. d. Deutschen chem. Gesellsch. **67**: 888-891 (May) 1934.
36. Karrer, Paul, and Fritzsche, H.: Fluorescenz-kurven des Lactoflavins und synthetischer Flavine, Helvet. chim. acta **18**: 911-914 (May) 1935.
37. Kuhn, Richard, and Rudy, Hermann: Ueber die optische Aktivität des Lacto-flavins, Ber. d. Deutschen chem. Gesellsch. **68**: 169-170 (Jan.) 1935.
38. Karrer, Paul, and Fritzsche, H.: Die optische Aktivität des Lactoflavins, Helvet. chim. acta **18**: 1026-1027 (June) 1935.
39. Karrer, Paul; Salomon, H.; Schöpp, K.; Schlittler, E., and Fritzsche, H.: Ein neues Bestrahlungsprodukt des Lactoflavins: Lumichrom, Helvet. chim. acta **17**: 1010-1013 (Oct.) 1934.
40. Kuhn, Richard, and Moruzzi, Giovanni: Ueber das Reduktions-Oxydations-Potential des Lacto-flavins und seiner Derivate, Ber. d. Deutschen chem. Gesellsch. **67**: 1220-1223 (July) 1934.
41. Stern, K. G.: Potentiometric Study of Photo-flavins, Biochem. J. **28**: 949-964 (March) 1934.
42. Kuhn, Richard, and Wagner-Jauregg, Theodor: Ueber das Reduktions-Oxydations-Verhalten und eine Farbreaktion des Lacto-flavins (Vitamin B_2), Ber. d. Deutschen chem. Gesellsch. **67**: 361-363 (Feb.) 1934.
43. Stern, K. G.: Uroflavin, Maltoflavin and Redox-Potentials of Lyochromes, Nature **133**: 178-179 (Feb. 3) 1934.
44. Kuhn, Richard, and Ströbele, Rudolf: Ueber Verdo-, Chloro- und Rhodo-flavine, Ber. d. Deutschen chem. Gesellsch. **70**: 753-760 (April) 1937.

imately the same wavelength regions. It is apparent, therefore, that this property resides in the tricyclic chromophore nucleus of the flavins. Riboflavin exhibits definite maxima at approximately 220, 267, 366 and 446 millimicrons. The green fluorescence extends from about 500 to 630 millimicrons. The use of the extinction coefficient especially in connection with the wavelength maximum at 267 millimicrons is useful in measuring the relative purity of riboflavin preparations.

Flavin Combination in Natural Products.—At least 90 per cent of the riboflavin in milk is in a free dialysable form. In most other materials, such as liver, yeast and green leaves, it occurs in combination with compounds of high molecular weight.[45]

VITAMIN ACTIVITY OF RIBOFLAVIN

No fewer than a dozen reports have appeared which carried some semblance of a quantitative relationship between riboflavin dosage and the growth rate of rats on a riboflavin-deficient diet. In many cases, however, such meager data were supplied in these reports relative to the control of the experimental animals that critical examination of the work is impossible. It would seem probable that no two groups of workers had used



XIII. Yellow oxidation enzyme (Warburg).

the same riboflavin-deficient diet and probably most of them had not completely eliminated the practice of coprophagy in the experimental animals. The action of micro-organisms is responsible for the formation of flavin in the lower colon.

Kuhn and his co-workers [12] have reported that 7 micrograms of riboflavin was equivalent to a Bourquin-Sherman unit when the Bourquin-Sherman Vitamin G-deficient diet [8] was supplemented with vitamin B_4. In other words, they state than 7 micrograms of pure riboflavin will support a growth rate of 3 Gm. a week in standardized rats receiving this modified Bourquin-Sherman diet.

Von Euler and his co-workers,[46] using a somewhat different diet, report that 2 micrograms of riboflavin correspond to a Bourquin-Sherman unit.

In my experience (unpublished data), 3 micrograms of crystalline riboflavin per rat daily as a supplement to the Bourquin-Sherman diet regularly induced a weekly growth rate of 3.1 ± 1.0 Gm. The practice of coprophagy in these experiments was completely eliminated and the vitamin G-deficient diet was prepared as originally described by Bourquin and Sherman.

45. Kuhn, Richard, and Kaltschmitt, Hans: Ueber den Zustand des Vitamins B_2 in der Kuhmilch, Ber. d. Deutschen chem. Gesellsch. **68:** 386-387 (Feb.) 1935.

46. von Euler, H.; Karrer, Paul; Adler, E., and Malmberg, M.: Ueber die Wachstumswirkung der Flavine, Helvet. chim. acta **17:** 1157-1165 (Oct.) 1934.

The riboflavin requirements are closely related to body size or more particularly to mass of active tissue, a further fact which may help to explain some of the divergence in vitamin values reported for riboflavin.

RELATION OF RIBOFLAVIN TO THE YELLOW ENZYME

The yellow oxidation enzyme discovered by Warburg and Christian has been isolated in crystalline form by Theorell.[47] This isolation was accomplished by a combination of cataphoresis and fractionation with ammonium sulfate. Cataphoresis was used principally to separate the enzyme from large amounts of polysaccharides, which would interfere with the subsequent fractionation.

The reversible splitting of the protein and riboflavin components of this enzyme was accomplished by dialysis against dilute hydrochloric acid followed by dialysis against water. By mixing the electrolyte-free water solutions of the components in the cold, the activity of the enzyme for the most part returned.[47]

The molecular weight of the enzyme as calculated by Kerwick and Pedersen [48] from the sedimentation and diffusion data, sedimentation equilibrium data and assuming that the enzyme contains one molecule of riboflavin (molecular weight 376) per molecule of enzyme, gave values in the neighborhood of 80,000. The iso-electric point of the enzyme was found to be about p_H 5.2.

Theorell [49] furthermore found that riboflavin existed in the enzyme as a phosphoric acid ester, a nucleotide combination in which the purine is replaced by riboflavin. Kuhn and his co-workers [50] have succeeded in synthesizing the riboflavin-5′-phosphoric acid ester (6,7-dimethyl-9-d-riboflavin-5′-phosphoric acid) and find it identical with cytoflav from heart muscle. The phosphoric acid radical is, in fact, one of the connecting links between the riboflavin and the protein component of the enyzme. It has been postulated [51] that the protein component of the enzyme is bound to the phosphoric acid radical and to the free imide group in position 3 of the riboflavin-5′-phosphoric acid ester. Riboflavin itself is much less effective than its phosphoric acid ester in combining with the protein component, while a blocking of the hydrogen atom of the imide group in position 3 prevents the combination of protein and flavin components. Kuhn and his co-workers have, as a result of these observations, expressed the combination of protein and riboflavin phosphoric acid ester as shown in formula XIII. A less active enzyme is formed by combination of riboflavin (unesterified) and the protein component solely through the imide grouping of the former at position 3. This combination is broken by dialysis against distilled water at p_H 7.0.

The yellow oxidation enzyme contains 15.9 per cent of protein and 0.043 per cent of phosphorus. It also possesses at least three distinct absorption maxima at wavelengths of 265, 380 and 465 millimicrons. For

47. Theorell, Hugo: Reindarstellung (Kristallisation) des Gelben Atmungsfermentes und die reversible Spaltung desselben, Biochem. Ztschr. **272:** 155-156 (July) 1934.

48. Kerwick, R. A., and Pedersen, K. O.: Some Physicochemical Characteristics of the Yellow Respiratory Enzyme, Biochem. J. **30:** 2201-2205 (Dec.) 1936.

49. Theorell, Hugo: Ueber die Wirkungsgruppe des Gelben Ferments, Biochem. Ztschr. **275:** 37 (Dec.) 1934.

50. Kuhn, Richard; Rudy, Hermann, and Weygand, Friedrich: Ueber die Bildung eines kunstlichen Ferments aus 6, 7-dimethyl-9-1-araboflavin-5′-phosphorsäure, Ber. d. Deutschen chem. Gesellsch. **69:** 2034-2036 (Sept.) 1936.

51. Kuhn, Richard, and Rudy, Hermann: Katalytische Wirkung der Lactoflavin-5′-phosphorsäure, synthese des Gelben Ferments, Ber. d. Deutschen chem. Gesellsch. **69:** 1974-1977 (Aug.) 1936.

further details of the chemical and enzymatic properties of this enzyme the reader is referred to the review by Theorell.[52]

The role of riboflavin as a component of an oxidation enzyme present presumably in all living cells explains some of the observations which were so baffling only a few years ago. Animals subsisting on riboflavin-deficient diets for any considerable period were invariably in a more critical condition than outward and obvious signs could indicate. They appeared for quite some time before death to be on the verge of collapse. This condition would seem to be a necessary corollary to the cellular asphyxiation brought about by a lack of a cellular oxidation catalyst.

SUMMARY

Riboflavin (6,7-dimethyl-9- [d-l'ribityl] -iso-alloxazine) is a yellow green-fluorescent water-soluble pigment widely distributed throughout both the plant and the animal kingdoms.

Through its iso-alloxazine nucelus it is related to and possesses a combination of the chemical properties of a substituted benzene, an azine dye and a pyrimidine. In addition, riboflavin possesses a ribityl side-chain attached to the N-atom in position 9, which relates it to the pentose sugars.

Riboflavin forms a phosphoric acid ester (riboflavin-5'-phosphoric acid) which combines with a protein to yield a yellow oxidation enzyme. This enzyme is presumably present in every living cell, at least in the cells of all higher forms of life, and is concerned with the chemical reactions involved in cell respiration.

52. Theorell, Hugo: Das Gelbe Oxidationsferment, Biochem. Ztschr. **278**: 263-290 (June) 1935.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORT.

HOWARD A. CARTER, Secretary.

WESTERN ELECTRIC 3-A ELECTRICAL STETHOSCOPE ACCEPTABLE

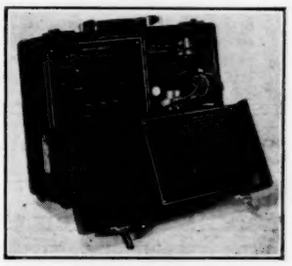
Manufacturer: Western Electric Company, 195 Broadway, New York.

This portable electrical stethoscope is designed to aid the physician in hearing heart sounds and in diagnosing heart ailments. It has been developed particularly for physicians with impaired hearing, according to the firm. However, it is equally recommended as useful to the physician with normal hearing in examining thick-chested individuals or detecting heart conditions during their early stages. It is claimed by the firm that other useful applications will be found in obstetric and lung fields.

Readily portable, the instrument is housed in a small fabrikoid carrying case, 12½ by 8¾ by 4¾ inches, weighing approximately 14 pounds. This contains the entire equipment, consisting of tubes and electrical wiring, six dry cell batteries and a space containing the microphone, receiver and cable. Provision is made for an additional receiver to be connected with the stethoscope so that two physicians may listen to heart sounds from the same patient simultaneously.

The Electrical Stethoscope essentially consists of a sensitive microphone, a vacuum tube amplifier and a receiver to reproduce the sounds. The two-stage amplifier, operated by dry batteries, will increase the loudness of the heart sounds about 20 decibels, or 100 times the intensity obtained with an ordinary acoustical stethoscope. The amplifier has a maximal gain of 60 decibels. Its frequency gain characteristic is essentially flat over a range in excess of that covered by the pick-up. This pick-up is unresponsive to extraneous sounds and has a frequency range running from 60 to 1,500 cycles, which covers the frequency range of heart sounds, according to the firm. It contains a filter which may be cut in or out of the circuit by means of a switch located on the front of the instrument, accentuating murmur sounds. The filter control diminishes the response at both the low and high frequencies. Thus the intensity of normal heart sounds is lowered and the loudness of any existing murmurs is accentuated by the isolation.

The batteries are stored in the two bottom compartments of the chasses. These are a filament battery, consisting of four flashlight cells No. 950 and two No. 768 plate batteries. The latter are of the plug-in type, with their terminals attached to receptacles mounted in the top of the battery. This simplifies replacement, since the leads used to connect them terminate in polarized plugs, so that they cannot be incorrectly inserted.



Western Electric 3-A Stethoscope.

Like the pick-up, the telephone type receiver is provided with a special cap to allow attachment of the tubes of an acoustic stethoscope. These tubes modify the quality of the sounds heard and are employed with this instrument instead of headphones so that the sounds heard will be as nearly as possible like those heard with the usual stethoscope.

A single volume control is provided which turns the amplifier off at the extreme left position and gives increased volume when turned to the right. The filter switch is the only other control and is used only when murmurs are suspected.

The unit was investigated in a clinic satisfactory to the Council. It was reported that the instrument distorts in a measure the heart and breath sounds so that a certain amount of experience is necessary to learn the normal sounds as produced by it. It did not appear to bring to light murmurs that are inaudible to the ordinary stethoscope.

In view of the foregoing report the Council on Physical Therapy voted to include the Western Electric 3-A Stethoscope in its list of accepted devices.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

THE FOLLOWING ADDITIONAL ARTICLES HAVE BEEN ACCEPTED AS CONFORMING TO THE RULES OF THE COUNCIL ON PHARMACY AND CHEMISTRY OF THE AMERICAN MEDICAL ASSOCIATION FOR ADMISSION TO NEW AND NONOFFICIAL REMEDIES. A COPY OF THE RULES ON WHICH THE COUNCIL BASES ITS ACTION WILL BE SENT ON APPLICATION.

PAUL NICHOLAS LEECH, Secretary.

SULFANILAMIDE-LILLY (See THE JOURNAL, Oct. 23, 1937, p. 1365; and Revised Supplement to New and Nonofficial Remedies, 1937, p. 29).

The following dosage form has been accepted:

Sulfanilamide Tablets, 7½ grains.

SILVER NITRATE (See New and Nonofficial Remedies, 1937, p. 431).

Ampoules Silver Nitrate Solution, 1 per cent-Abbott: Each wax ampule contains approximately 0.5 cc. of a solution of silver nitrate, U. S. P., 1 per cent in chemically pure water. For the prevention of ophthalmia neonatorum, two drops of the solution are instilled under the lower lid of each eye of the new-born after suitable cleansing.

Prepared by the Abbott Laboratories, North Chicago, Ill. No U. S. patent or trademark.

PROCAINE-ABBOTT (See New and Nonofficial Remedies, 1937, p. 69).

The following dosage form has been accepted:

Procaine Hydrochloride, ⅓ grain-Epinephrine, 1/4,000 grain Hypodermic Tablets: Each contains procaine hydrochloride-Abbott 0.02 Gm. (⅓ grain), epinephrine 0.000016 Gm. (1/4,000 grain), sodium bisulfite 0.0016 Gm. (1/40 grain) and sodium chloride sufficient so that when the tablet is dissolved in 1 cc. of water the resulting solution is approximately isotonic.

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SATURDAY, APRIL 2, 1938

WHEELER-LEA BILL GIVING FEDERAL TRADE COMMISSION JURISDICTION OVER FOODS, DRUGS, DEVICES AND COSMETICS BECOMES A LAW

Unfair and deceptive acts and practices in the exploitation and sale of foods, drugs, diagnostic and therapeutic devices and cosmetics in interstate and foreign commerce, even though not involved in commercial competition, will shortly come under the jurisdiction of the Federal Trade Commission through the operation of the Wheeler-Lea Act,[1] approved March 21 by the President. The act becomes effective on the expiration of sixty days immediately following the date of its approval. The jurisdiction of the Federal Trade Commission over unfair and deceptive acts and practices is now limited to such as constitute or form a part of unfair methods of commercial competition. The act just approved will give the commission, too, specific jurisdiction over the advertising of foods, drugs, diagnostic and therapeutic devices and cosmetics, whenever such advertising is disseminated in interstate and foreign commerce. Advertising that is disseminated or displayed only locally will come within the jurisdiction of the commission if it is designed to promote interstate and foreign commerce in the goods advertised. Only in event of proved danger to health or deliberate fraud will the offender be liable to fine and imprisonment. Under all other conditions, he will be subject only to a money penalty, to be recovered by civil suit, and then only after he has ignored a cease and desist order issued by the commission. A cease and desist order can be issued only after notice and hearing, with the right of appeal to the courts, a process that will normally occupy not less than ninety days. Appeals to the courts may possibly delay its effectiveness over a period of years.

After the new act becomes effective, no person, except as specifically stated, can lawfully disseminate any false advertisement of any food, drug, diagnostic or therapeutic device or cosmetic by mail. No one can disseminate such an advertisement in interstate or foreign commerce by any means to induce the purchase of the merchandise named. Neither can any one disseminate a false advertisement even locally if it is designed to induce the purchase of such merchandise in interstate or foreign commerce. A "false advertisement" within the meaning of the act is any advertisement, other than labeling, that is misleading in a material respect. In determining whether an advertisement is or is not misleading, the commission must take into account not only representations made or suggested in it but also the extent to which it fails to reveal facts material in the light of such representations, or facts that are material with respect to the consequences which may result from the use of the commodity to which the advertisement relates, under the conditions prescribed in the advertisement or under such conditions as are customary or usual. In the case of a drug, however, no advertisement is to be deemed false that is disseminated only to the members of the medical profession, contains no false representation of a material fact, and includes or is accompanied in each instance by a truthful disclosure of the formula, showing quantitatively each ingredient. Publishers, radio broadcast licensees, and agencies or mediums for the dissemination of advertising, except the manufacturer, packer, distributor or seller of the commodity to which the false advertisement relates, are to be immune from punishment if they disclose, on request of the Federal Trade Commission, the name and post office address of the manufacturer, packer, distributor, seller or advertising agency in the United States that caused the dissemination of the false advertisement.

False advertising is to be regarded ordinarily as an unfair or deceptive act or practice and proceeded against by notice, hearing and the issue of a cease and desist order, subject to appeal to the courts. If, however, the commodity advertised may be injurious to health because of results from use under the conditions prescribed in the advertisement or under such conditions as are customary or usual, or if the advertisement is disseminated with intent to defraud or mislead, the advertiser may be prosecuted criminally without previous notice and fined and imprisoned. If the Federal Trade Commission believes that any person, partnership or corporation is disseminating or about to disseminate any false advertisement of a food, drug, diagnostic or therapeutic device or cosmetic and that the interest of the public requires that the dissemination of that advertisement be prevented or suspended pending final action by the commission, the commission may appeal to the court for an injunction or restraining order, which may be issued if it does not delay the delivery of any particular issue of a newspaper, magazine, periodical or publication, published at regular intervals, provided the publisher has not, in order to evade the requirements of the act, purposely concealed the misleading character of the advertisement so long

1. Public—No. 447—75th Congress, An Act to amend the act creating the Federal Trade Commission, to define its powers and duties and for other purposes.

that any change necessary to make it truthful would delay publication of the periodical.

The provisions of the new act that relate to advertising originated in bills designed to safeguard the public against fraud and danger to health through the distribution in interstate and foreign commerce of adulterated and misbranded foods, drugs, diagnostic and therapeutic devices and cosmetics. The advertising provisions in the present act were lifted bodily from the Copeland food and drugs act, S. 5, which has passed the Senate, and, after modification, were included in the act which has just been approved. Jurisdiction over the advertising of foods, drugs, diagnostic and therapeutic devices and cosmetics is therefore to be vested in the Federal Trade Commission, while jurisdiction over the labeling of such products will be left to the Secretary of Agriculture. There will be similar division of authority with respect to the general control of such merchandise. While the Secretary of Agriculture is still to retain specific control over adulteration and misbranding, the Federal Trade Commission can at any moment take jurisdiction on the ground that adulteration and misbranding constitute unfair or deceptive acts or practices and therefore come within its jurisdiction. Inevitably such division of authority with respect to labeling and advertising and such duplication of authority with respect to adulteration and misbranding will lead to conflicts. The enlarged jurisdiction of the Federal Trade Commission will necessitate an increase in personnel and laboratory resources, if effective work is to be done. The public should be aware of the situation and the medical profession must continue to investigate and to protect the public until it is satisfied that this act as administered is affording the protection that is required.

A NEW SOURCE OF BLOOD FOR TRANSFUSION

The theory that fetal blood possesses a high immunobiologic antiblastic quality against neoplasms caused Bruskin and Farberova [1] of the Oncologic Institute of Moscow to attempt the use of placental blood for massive transfusions during surgical treatment of malignant neoplasms. The blood was obtained from the umbilical vein and the placenta of the new-born. The amount obtainable from one placenta varied between 50 and 120 cc. It was found that the hemoglobin of the placental blood varied from 90 to 120 per cent (the method of determination not stated), erythrocytes from 5,000,000 to 6,000,000, and leukocytes from 8,000 to 16,000, with a definite lymphocytosis (from 32 to 46 per cent). The reticulocytes varied from 11 to 30 in 1,000 cells. The observers believe that placental blood contains a number of hormones of ovarian and anterior pituitary origin. The blood was conserved for from six to ten days. Bruskin and Farberova estimate that two thirds of the 60,000 annual births in Moscow could be used for the provision of placental blood. An average of 50 cc. from each birth would yield 2,000 liters, or an amount sufficient for from 6,000 to 8,000 blood transfusions.

Stavskaya [2] reported in 1937 on the use of retroplacental blood in the obstetric-gynecologic clinic of the Mother and Child Institute in Kiev. She likewise emphasized the distinguishing characteristics of the placental blood to be its high hemoglobin content, increased morphologic elements, considerable content of bilirubin, high sugar content, and low cholesterol and alkali reserve. The blood contains estrogen, gonadotropic substance and an epinephrine-like substance. It is also distinguished by its rapid coagulability. The amount of blood obtainable from a retroplacental hematoma varied from 80 to 300 cc. The isoaggulatination properties of the placental blood are sharply defined and the blood grouping corresponds always to that of the mother's blood. Stavskaya found that the placental blood in vitro has little tendency to coagulate and may be kept without preservatives for from ten to twelve days.

Goodall, Anderson, Altimas and MacPhail [3] have demonstrated that emptying the placenta of its blood does not appreciably influence either the time of its separation or its completeness. They have adopted much the same technic as did the Russian workers and confirmed all of the advantages claimed for the method. They have adopted, after some experimentation, a preservative proposed by the Moscow Institute of Hematology and consisting of sodium chloride 7 Gm., sodium citrate 5 Gm., potassium chloride 0.2 Gm., magnesium sulfate 0.004 Gm., and bidistilled water 1,000 cc. They found that it was not necessary to take cultures of the preserved blood because contamination does not take place at the low temperature at which the blood is preserved. Slightly progressive hemolysis was found to occur after the first fifteen days. This, however, they found to be no barrier to a normal transfusion. The reason for the innocuousness of this hemolysin lies in the fact that the hemolysin is small in quantity and is apparently inoperative in the recipient. They comment on the fact that the polycythemia of a child at birth leads to the destruction of a number of red cells when the lungs come into operation. The breaking down of these cells is the cause of many of the cases of hemolytic jaundice in the newborn. They advance this explanation to meet the argument that taking of blood from the placenta deprives the new-born infant of its rightful due. They found also that fetal blood contains from 20 to 35 per cent

1. Bruskin, Ya. M., and Farberova, R. S.: Use of Umbilical and Placental Blood for Massive Transfusions in Surgery, Sovet. vrach. zhur. **40:** 1546 (Oct. 30) 1936; abstr. J. A. M. A. **107:** 2098 (Dec. 19) 1936.

2. Stavskaya, E.: Transfusion of Placental and Retroplacental Blood, Novy khir. arkhiv. **37:** 72, No. 145, 1937; abstr. J. A. M. A. **108:** 1226 (April 3) 1937.

3. Goodall, J. R.; Anderson, F. O.; Altimas, G. T., and MacPhail, F. L.: An Inexhaustible Source of Blood for Transfusion and Its Preservation, Surg., Gynec. & Obst. **66:** 176 (Feb.) 1938; abstr. this issue, p. 1148.

more coagulation power than that of adult blood. This appears to be nature's provision to prevent exsanguination of the new-born in animals in which the cord is torn or bitten. This property presents an advantage in transfusion for hemorrhage. The authors feel that preserved blood has many advantages over fresh blood. It eliminates food and other extraneous allergic reactions. In many transfusions there did not occur a single untoward reaction or rise of temperature. Two or more fetal bloods may be given simultaneously if necessary after separate matching. They suggest that a maternity section of a general hospital is capable of giving more than enough blood for the needs of the whole institution and that the blood can be sent to other institutions in adequate vacuum containers if the group of the recipient is known. The method appears to be an efficient and inexhaustible source of blood for transfusion.

SYNERGIC EFFECTS OF ANTIGENS

When two or more simple antigens are injected simultaneously into laboratory animals, the usual antibody response may be modified. This modification may be a suppression, perversion or augmentation of specific antibody formation against one or more of the individual antigens. The earliest description of this phenomenon was the observation by Burky and his co-workers [1] at Johns Hopkins University that rabbit lens proteins are not antigenic for rabbits but that the lens protein complex can be rendered antigenic by simple fractionation. The alpha fraction causes high titer precipitin production in rabbits. While both the beta and gamma fractions are antigenically inactive, each has the property of suppressing antibody production against alpha proteins.

A teleological explanation of this relationship might assume that the crystalline lens had developed a protective mechanism consisting of specific inhibins and that the absorption or internal secretion of these inhibins prevent the formation of antigens precipitin which otherwise might cause degenerative changes in the eye. If this explanation is correct, a biologic theorist would postulate the existence of similar local antigenic inhibins in other highly specialized organs or tissues, particularly the endocrine glands. Endocrine therapy is often self limiting because of the antigenicity of available preparations of hormones. The resulting antiendocrine immunity not only limits therapeutic action but may lead to autotoxic degeneration of homologous endocrine glands.

Of even greater clinical promise is the opposite phenomenon, the augmentation of antibody response in certain mixed antigens. Burky [2] for example found that, while pollen extracts are practically nonantigenic for rabbits, high-titer antibodies can be produced against pollens if they are "synergized" or "potentiated" by the addition of staphylococcus toxin. Swift and Schultz [3] of the Rockefeller Institute have confirmed this observation and have found that it is not necessary to mix the staphylococcus toxin with the nonantigenic protein before injection. The two may be injected independently, as by different routes or at different times, and still produce augmented antibody response. They also found several substances other than staphylococcus toxin that can function as antigenic energizers.

Among the latest confirmations of the Burky phenomenon are the observations by Magerl [4] of the Hygienic Institute at the University of Innsbruck, who studied the synergic antigenicity of different blood mixtures. Magerl found that horse, ox, swine and sheep erythrocytes would each cause prompt production of specific amboceptor in rabbits but a mixture of two or more specimens of blood is often relatively nonantigenic. Other mixtures, such as of sheep and horse erythrocytes, cause about ten times the normal antibody response. The amboceptors appear more promptly, are of higher titer and persist longer than in the control injections with individual sheep or horse blood.

Apparently an attempt has not yet been made to formulate a theory as to the chemical or physiologic mechanism by which these antigenic mixtures inhibit or augment antibody synthesis. The discovery of these two synergic phenomena, however, stimulates hope of renewed clinical victories in many fields of vaccine therapy and serum therapy. A nonantigenic solution of posterior pituitary or a successfully "potentiated" tuberculin are not beyond the realm of possibility.

1. Burky, E. L., and Woods, A. C.: Arch. Ophth. **57**: 41 (Jan.) 1928. Woods, A. C.; Burky, E. L., and Woodhall, M. B.: Tr. Am. Opth. Soc. **29**: 168, 1931.
2. Burky, E. L.: J. Allergy **5**: 466 (July) 1934.
3. Swift, H. F., and Schultz, M. P.: J. Exper. Med. **63**: 703 (May) 1936.
4. Magerl, J.: Ztschr. f. Immunitätsforsch. u. exper. Therap. **90**: 327 (May 27) 1937.

Current Comment

COMMERCIAL ASPECTS OF J. THOMPSON STEVENS—A "MIRACLE MAN"

In the *Cosmopolitan* for March 1938 Mr. Rex Beach, pursuing his devious course through his conception of the great prophets in medicine, devotes some space to the work of Dr. J. Thompson Stevens of New York City and lists him with the "Modern Miracle Men." Among the previous inhabitants of niches in Mr. Rex Beach's hall of medical fame are Mahlon Locke of Canada, Hiss of California and a number of nondescript faith healers and promoters of unestablished methods of more or less scientific disrepute. The selection of Dr. Stevens would seem to be extraordinary, since he is listed as a member of the Radiological Society of North America and of the American Roentgen Ray Society as well as of the New York State Medical Society and the New Jersey State Medical Society. A brief analysis of the article by Mr. Beach indicates that Dr. Stevens is, in Mr. Beach's opinion, capable of performing miracles in the healing of infections of the sinuses and in the removal of the tonsils by the use of the roentgen ray. The scientific evidence available as to these perform-

ances is obviously not such as to support these contentions. What appears to be an unusual feature of this exploitation of Dr. Stevens is the development of a commercial setup for suitable exhaustion of the available profits from this type of promotion. In some manner a young woman called Miss Phoebe Elkins seems to be associated with the promotion. Characterizing herself as a publicity woman, she has called on physicians indicating that it is her business to arrange publicity for doctors and that she aided Mr. Beach in finding Mahlon Locke and Stevens for his literary purposes. Writing on the stationery of Dr. Stevens, she indicates also that she arranges medical consultations for people who are attracted by the articles in the magazine either with the "hero" of the article by Mr. Beach or with associates in neighboring cities:

"We are greatly in need of a good diagnostician and Roentgenologist to become affiliated with us in your vicinity. As you undoubtedly know Dr. Stevens is considered one of the finest Roentgenologists in the East and because of his ability we are deluged with requests for an associate in various parts of the country. From what I understand you fill the above qualifications. Therefore, I am wondering if you would enjoy an affiliation in your vicinity with our main offices, namely, New York City and Montclair, New Jersey."

These, it appears, will be asked to treat the patients and then remit to her one third of the gross amount to be received from such treatments. The physician who supplies the information concerning his contact with Miss Elkins was offered the concession in a neighboring city and was informed that there was some $25,000 worth of business which had been developed by the publication of Mr. Beach's article. As we go to press information is received indicating that the astute promoters are also recommending application of the x-rays for the control of goiter. Obviously this entire performance smells to high heaven from an ethical point of view. The public needs protection against such unwarranted commercial exploitation. Incidents of this type are the actual proof of the necessity for principles of ethics to control advertising and exploitation of physicians.

THIAMIN CHLORIDE AND NICOTINIC ACID IN PELLAGRA

Elsewhere in this issue (page 1081) is an article by Spies and Aring on the effect of the administration of vitamin B_1 on the peripheral neuritis of pellagra. Observations are recorded in six cases of classic pellagra with peripheral neuritis, in four of which pellagra had developed after alcohol had been largely substituted for a balanced dietary. Irrespective of the cause of the pellagra, prompt relief of spontaneous neuritic pain resulted from the intravenous injection of thiamin chloride (crystalline vitamin B_1 hydrochloride). These observations suggest that vitamin B_1 deficiency plays a part in the development of clinical manifestations of peripheral neuritis associated with pellagra. Since some patients fail to absorb vitamin B_1 by mouth, it seems to be necessary to give them parenteral injections. The vitamin B_1 does not appear to cure the glossitis and stomatitis of pellagra but nicotinic acid, which has been referred to in an editorial in THE JOURNAL [1] as well as in a recent article by Spies and his co-workers,[2] does relieve these symptoms. Taken together these interesting observations made by the Cincinnati investigators leave little doubt that pellagra, or at least some of its manifestations, is the result of more than one factor. They have demonstrated that all types are benefited within twenty-four to forty-eight hours after the administration of nicotinic acid. Certainly both thiamin chloride and nicotinic acid deserve further intensive study in their relation to pellagra.

GOVERNOR CHANDLER OF KENTUCKY GIVES HIGH PRAISE TO AMERICAN PHYSICIANS

Refreshing as a spring breeze is the following statement by Gov. A. B. Chandler of Kentucky at the dedication of a new wing of the State Tuberculosis Sanitarium at Hazelwood, Ky., March 28:

Kentuckians are very proud of the distinguished history of its medical profession. The first medical school in the West was Transylvania at Lexington, and no institution in this country made a greater contribution to the public health and welfare of its day.

Now, for more than a hundred years, those in charge of public affairs have left medical and health problems to the doctors. More progress has been made in public health and medical service than in any other human activity in Kentucky. I am convinced that this is because the responsibility for it has been placed squarely on the shoulders of the medical profession.

In the last fifty years, the death rate has been reduced two thirds; acute diseases have been reduced as much as in any other state; we have more full-time health departments than any other state. This organization has been entirely medical from its beginning, and its principles have been determined and its activities controlled by physicians of the state. We realize fully that our doctors have made the largest contribution in value to the welfare of our citizens of any group. So far as it has been possible for them to do so, they have given the same service to rich and poor alike. Seventy-five years ago the average age at death in Kentucky was 32 years; last year it was 61 years. This of course, means that many more people are living in the older groups.

We must realize that this older average population presents us with a tremendous problem; we must make the same study and take the same care of chronic and degenerative diseases that formerly we have so successfully accomplished with the infectious diseases.

Opportunists talk very glibly about health insurance, the socialization of medicine and the regimentation of physicians as the remedy for this situation. Such suggestions will receive no support by the people of Kentucky. We will continue to be guided in regard to public health and medical service by our doctors.

Recently Dr. Irvin Abell, President-Elect of the American Medical Association, has informed me of the study of medical service and the provision for medical care for the indigent, which study is being undertaken by the American Medical Association. He properly advances the concept that the organized medical profession is the family physician of the commonwealth and that it should examine the resources for medical service and that it should show exactly what they should do to obtain all the benefits of modern scientific medicine.

Realizing that the profession has been very busy in reducing the death rate from acute and infectious diseases, we will patiently await their examination and diagnosis in regard to

1. Pellagra and Nicotinic Acid, editorial, J. A. M. A. **110:** 289 (Jan. 22) 1938.
2. Spies, T. D.; Cooper, Clark, and Blankenhorn, M. A.: The Use of Nicotinic Acid in the Treatment of Pellagra, J. A. M. A. **110:** 622 (Feb. 26) 1938.

the medical conditions which confront us, and we will be guided by them with perfect confidence that they will continue to give our people all that modern science can give toward making Kentucky the healthiest, the happiest and the most effective people in these United States.

The medical profession is proud of this tribute to its record of the past, grateful for this judgment of what medicine is trying to do in the present, and appreciative of the confidence of Governor Chandler in medicine's future.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

State Medical Meeting at Mobile April 19-21. — The Medical Association of the State of Alabama will hold its annual meeting at the Battle House in Mobile, April 19-21, under the presidency of Dr. Edward S. Sledge, Mobile. The following speakers will participate:

Dr. Lawrence H. Hinton, Mobile, Review of Some External Eye Diseases.
Dr. James Otis Lisenby, Atmore, Diagnosis and Treatment of Tumors of the Breast.
Dr. Frank A. Kay, Tuscaloosa, Metrazol Treatment of the Psychoses.
Dr. Chalmers H. Moore, Birmingham, Head Injuries.
Dr. Joe H. Little, Mobile, Progress in the Treatment of Diabetes.
Dr. Benjamin F. Byrd, Nashville, Tenn., The Insurance Triangle: Applicant, Examiner, Company.
Dr. Robert S. Hill, Montgomery, Medicine as a Profession.
Dr. John H. Musser, New Orleans, Treatment of Organic and Inorganic Diseases of the Stomach.
Drs. John W. Means and Camille J. DeLor, Columbus, Surgery of Biliary Passages with Reference to the Hazards and Their Management.
Dr. Charles N. Leach, Montgomery, Rabies.
Dr. Albert Graeme Mitchell, Cincinnati, Practical Application of Studies on Gastro-Enteritis.
Dr. Henry F. Helmholz, Rochester, Minn., Abdominal Tumors in Childhood.
Dr. Oscar W. Bethea, New Orleans, The Pneumonias.

A symposium on obstetrics will be presented Tuesday evening by Drs. James R. Garber, Birmingham, and Archie E. Thomas, Montgomery. Dr. Thomas M. McMillan, Philadelphia, will deliver the Jerome Cochran Lecture Wednesday morning on "An Optimistic View of Some Problems of Heart Disease." Dr. Charles A. Mohr, Mobile, will open a public meeting Wednesday; the speakers will be Dr. Alice C. Evans, Washington, D. C., on "Undulant Fever as a Public Health Problem" and Dr. James N. Baker, state health officer, Montgomery, "What the State Department of Public Health Is Doing for the Citizens of Alabama." The thirteenth annual meeting of the Woman's Auxiliary to the state medical association will be held at the Cawthon Hotel in Mobile April 19-21. The thirteenth annual session of the Alabama Pediatric Society will be held at the Battle House April 18. The speakers will include Dr. Mitchell on "Is the Pediatrician a Psychiatrist?"; Dr. Helmholz, "Treatment of Acute Urinary Infections in Childhood"; Dr. Joseph Yampolsky, Atlanta, Ga., "A Comparative Review of the Drugs Used in the Treatment of Syphilis." Drs. Mitchell and Yampolsky will also address the evening session.

CALIFORNIA

Course on Diseases of Digestive Tract.—The University of California Medical School, San Francisco, will conduct a short graduate course in diseases of the digestive tract April 13-16. Instruction will be given by lectures, demonstrations and surgical clinics. The fee will be $20. Further information may be obtained from Dr. Langley Porter, dean of the medical school, Medical Center, San Francisco.

Society News.—A symposium on rabies was presented before the Pasteur Society of Central California March 3 in San Francisco by Drs. Jacob C. Geiger, director of health of San Francisco; Harry E. Foster, medical director, Cutter Laboratories, Berkeley, and Jacob Traum, M.S., professor of veterinary science, University of California.——Dr. Emile F. Holman discussed "Medicine in Scandinavia" before the San Francisco County Medical Society March 8 and Karl F. Meyer, Ph.D., "Medical Impressions from a Recent European Trip"; both talks were illustrated with colored slides.——Dr. Clifford B. Walker was recently elected president of the Los Angeles Society of Ophthalmology and Otolaryngology and Dr. John P. Lordan, secretary.——At a joint meeting of the Los Angeles County Medical Association with the Southern California Retail Druggists Association, March 17, Mr. Frank E. Mortensen, secretary of the latter group, among others, discussed "Prospective Legislation of Interest to Medicine and Pharmacy."——A round table discussion on "Treatment of Infection by Means of Small Doses of Insulin" was a feature of a joint dinner meeting of the Los Angeles Society of Ophthalmology and Otolaryngology and the Research Study Club of Los Angeles, March 28.

COLORADO

First Full Time Health Unit.—The first full time county health unit in Colorado was opened in Otero County February 7. Dr. Lynn J. Lull, formerly in private practice in Olathe, has been appointed health officer with headquarters at La Junta. The unit is maintained jointly by the county and the state in cooperation with the Otero County Medical Society. Plans are under way for the organization of a second unit.

CONNECTICUT

The Ferris Lecture in Anatomy.—Samuel R. Detwiler, Ph.D., professor of anatomy, Columbia University College of Physicians and Surgeons, New York, delivered the fifth Harry Burr Ferris Lecture at the Yale University School of Medicine, New Haven, March 2; his subject was "Vertebrate Visuo Receptors."

Society News.—Dr. Jerome M. Lynch, New York, will address the New England Proctologic Society in New Haven April 22 on "Lynch's Modification of the Perineal Operation." The society was organized in Hartford in November 1937 with Dr. Albert R. Keith, Hartford, president; Dr. Frederick S. Ellison, Hartford, secretary, and Dr. Simon B. Kleiner, New Haven, chairman of the executive committee.——Dr. Harry M. Zimmerman, New Haven, will address the Fairfield County Medical Association April 12 in Bridgeport on "Vascular Diseases of the Central Nervous System." Dr. Clarence L. Robbins, New Haven, will discuss "Edema, Its Differentiation and Treatment."

GEORGIA

Society News.—Dr. William G. Hamm, Atlanta, among others, discussed "Fractures of the Jaw" before the Fulton County Medical Society March 17. Dr. Edgar F. Fincher Jr., Atlanta, among others, presented a paper before the society, February 3, on "Sciatica and Low Back Pain—The Result of Ruptured Intervertebral Cartilage."

Dr. Warren Lectures in Atlanta.—Dr. Shields Warren, Boston, delivered a series of lectures at the Academy of Medicine, Atlanta, under the auspices of the Atlanta Clinical Society March 23-25. His subjects were "Recent Advances in the Pathology of Diabetes Mellitus," "Pathology of the Thyroid Gland" and "Radiosensitivity of Tumors."

ILLINOIS

Personal.—Dr. Robert H. Bell, health officer of Carlinville, has been appointed full-time superintendent of the district health unit composed of the counties of Scott, Morgan, Greene, Calhoun, Jersey and Macoupin.

Society News.—A joint meeting of the Mercer and Rock Island county medical societies in East Moline, March 8, was addressed by Drs. John S. Coulter, Chicago, on "Hyperpyrexia" and "Home Treatment of Chronic Arthritis with Physical Agents."——Dr. Paul H. Harmon, Chicago, addressed the Adams County Medical Society, Quincy, February 14, on "The Illinois Plan for the Care of Crippled Children."

Chicago

Dr. Joslin Will Address Medical Society.—Dr. Elliott P. Joslin, clinical professor of medicine, Harvard University Medical School, Boston, will address the Chicago Medical Society April 6 on "Present Conceptions of Diabetes Mellitus."

Dr. Pearl to Speak on Longevity. — Raymond Pearl, Ph.D., professor of biology, Johns Hopkins University School of Medicine and the School of Hygiene and Public Health, Baltimore, will deliver a public lecture at Thorne Hall, April 15, under the auspices of the Institute of Medicine of Chicago. The title of his lecture will be "Long Life and Living."

Society News.—Drs. Morris Fishbein, Editor, THE JOURNAL, and Rosco G. Leland, Director, Bureau of Medical Economics, American Medical Association, will address the

North Side Branch of the Chicago Medical Society at the Drake Hotel April 7, 8 p. m.; their subjects will be "Medicine and the National Policy" and "Hospital Service Plans" respectively.

Hospital Groups Merge.—The Chicago Hospital Association and the Chicago Hospital Council have been consolidated, the former to be the administrative section, according to the Chicago *Tribune*. Membership in the association was restricted largely to administrative heads of hospitals, while the council included superintendents, board presidents and chiefs of staff. The council had twenty-six member hospitals and the association twenty-three.

Measles Unusually Prevalent.—There were 24,363 cases of measles reported during the first seventy-six days of 1938, according to the Chicago *Tribune* March 21, recording a new high total for the city. This total was 164 more cases than that recorded for the entire year of 1935, the previous peak year. In the same period in 1937 only 259 cases were reported, while the total for the year was only 496, it was stated. The largest number of cases reported in a single day was 743 on March 10. Since the first of the year there have been twenty-one deaths attributed to measles, while in the same period in 1935 there were nineteen.

INDIANA

New Department Organized.—The creation of a new department of bacteriology and public health and a new department of pathology at Indiana University School of Medicine, Indianapolis, is announced. The former department of bacteriology and pathology was divided and bacteriology was combined with the division of public health. Dr. Thurman B. Rice, professor of bacteriology and public health, has been made chairman of the new department, and Dr. Frank Forry, professor of pathology, chairman of the new department of pathology. The pathology department has two divisions, one of general pathology with Dr. Forry as chairman and a division of clinical pathology with Dr. Clyde G. Culbertson as chairman, according to the Bloomington *Student*.

KENTUCKY

Personal.—Dr. Frank M. Rogers, formerly of Coleman, Ga., has been appointed health officer of Crittenden County with headquarters at Marion.——Dr. Michael M. Hall, Campbellsville, was appointed coroner of Taylor County to succeed the late Dr. Benjamin T. Black.——Dr. Elmer K. Umberger, formerly of Trinity, Texas, has been appointed health officer of McCreary County.

Dr. Abell to Receive Notre Dame Medal.—The Laetare Medal, awarded annually by the University of Notre Dame, is to be awarded to Dr. Irvin Abell, Louisville, President-Elect of the American Medical Association. In the announcement Father John O'Hara, president of the university, said:

> The merit of Dr. Abell in his profession has been signally recognized in his election to the presidency of the American Medical Association, and his varied service to city, state and nation, as surgeon, citizen, soldier and Christian gentleman, has endeared him in the esteem of a numerous and extensive public benefited by his years of devotion to the complete welfare of his fellow men.

The Laetare Medal was originated by Notre Dame in 1883 and Dr. Abell is the fifty-sixth recipient.

Society News.—Dr. Emmet F. Horine addressed the Louisville Medico-Chirurgical Society, March 11, on "Mercurial Diuretics."——A symposium on diseases of the gallbladder was presented before the Boyle County Medical Society, Danville, February 15, by Drs. John Rice Cowan, George M. McClure, Stuart P. Hemphill, Oscar L. May and S. B. Sharp, D.D.S., all of Danville.——At a quarterly meeting of the Southwestern Kentucky Medical Association in Benton February 8, Drs. George F. Cummins, Metropolis, Ill., and Earnest R. Goodloe, Paducah, spoke on "Clinical Findings in Thyroid Deficiency" and "Episiotomy—How, When and Why" respectively.——Dr. Arthur B. Barrett, Lexington, addressed the Bourbon County Medical Society, Paris, January 27 on "Endocrinology in Obstetrics and Gynecology" and George R. Smith, Lexington attorney, on "Medical Aspects of the Workmen's Compensation Act."

MAINE

Society News.—Dr. Maxwell Finland, Boston, discussed "The Treatment of Pneumonia" before the Cumberland County Medical Society February 25.——At a recent meeting of the Portland Medical Club Dr. Francis W. Hanlon spoke on "The Relation Between Acute Visceral Infections and the Alarm Reaction." Dr. Thomas Tetreau addressed the club recently on "Milk as a Factor Influencing the Infant Mortality Rate in Portland."——The Kennebec County Medical Association was addressed in Waterville February 17 on "Recent Developments in the Diagnosis and Treatment of Diseases of the Stomach."——At a meeting of the Penobscot County Medical Association in Bangor recently Dr. Champ Lyons, Boston, spoke on "Modern Methods in the Treatment of Pyogenic Infections."

MARYLAND

Society News.—At a meeting of the Baltimore City Medical Society, March 4, a paper by Drs. John E. Howard and Samuel A. Vest Jr. was presented by Dr. Vest; the subject was "Clinical Experiments in the Use of Testosterone." Dr. Herbert Schoenrich discussed "Sulfanilamide in Clinical Gonorrhea."——Dr. Thomas Nelson Carey, Baltimore, addressed the Carroll County Medical Society in Westminster January 26 on "Use of Serum in Treatment of Pneumonia."——Dr. Joseph H. Barach, Pittsburgh, addressed the Allegany-Garrett County Medical Society at Cumberland, February 25, on "Science of Nutrition and the Treatment of Diabetes."

The De Lamar Lectures.—The remaining lectures in the De Lamar series at the Johns Hopkins University School of Hygiene and Public Health, Baltimore, will be delivered by:

> Dr. Thomas Francis Jr., International Health Division of the Rockefeller Foundation, New York, April 12, The Immunology of Epidemic Influenza.
>
> Edmund V. Cowdry, Ph.D., professor of cytology, Washington University School of Medicine, St. Louis, April 19, Cellular Changes in Leprosy.
>
> Dr. Franz Weidenreich, honorable director, Cenozoic Research Laboratory, National Geological Survey of China, Sinanthropus Pekinensis and Its Significance for the Problem of Human Evolution. The date of this lecture had not been decided.

Robert Matheson, Ph.D., professor of economic entomology, Cornell University Agricultural Experiment Station, gave a lecture in this series March 8 on "Biology of Anophelines with Special Reference to Those of North America."

MICHIGAN

New Professor of Pathology.—Dr. Edgar H. Norris, Minneapolis, teaching assistant in pathology, University of Minnesota Medical School, Minneapolis, has been appointed professor and head of the department of pathology at Wayne University College of Medicine, Detroit, according to the Minneapolis *Journal*. The appointment is effective next fall. Dr. Norris graduated at the University of Minnesota Medical School in 1919.

Physicians Honored.—Dr. Heman B. Kiehl, Lapeer, was given a dinner by the Lapeer County Medical Society February 10 to observe his completion of more than fifty years in the practice of medicine. He was presented with a chair. Dr. Kiehl helped to organize the Ogemaw, Montmorency, Crawford, Oscoda, Roscommon and Otsego Medical Society, serving as vice president at the time of its establishment. He was formerly health officer of Rose City and is an alumnus of the College of Physicians and Surgeons, Keokuk, Iowa, class of 1887.——Dr. Robert B. Armstrong, Charlevoix, was recently chosen the first life member of the local Kiwanis Club; he was mayor of Charlevoix in 1907.——The Jackson Academy of Medicine and Dentistry gave a dinner in honor of Dr. Joseph C. Kugler in Jackson, January 27, to mark his retirement from active practice; Dr. Horace W. Porter, Jackson, was toastmaster.

MINNESOTA

Janitor Performs Illegal Operation.—Frank Kish, a janitor, pleaded guilty in Ramsey County March 1 to a charge of performing an abortion and was sentenced to a term of eighteen months at hard labor in a state penal institution. Kish admitted having performed about twenty-five abortions, charging from $5 to $30. He had only an eighth grade education and no medical training whatever, the state board of medical examiners reported.

Society News.—The Minnesota Pathological Society was addressed in Minneapolis March 15 by Dr. Abe B. Baker on "Subdural Hematoma" and Drs. Arild E. Hansen and Irvine McQuarrie and Mildred R. Ziegler, Ph.D., on "Disturbances in the Osseous and Lipid Metabolism in a Child with Primary Carcinoma of the Liver."——The Minnesota Academy of Medicine was addressed in St. Paul March 9 by Drs. Frederic E. B. Foley on "Operative Division of a Unilateral Fused Kidney" and Hendrie Grant, on "Malignant Hypertension."——Dr. George R. Dunn has been elected president of the Minneapolis Surgical Society, succeeding Dr. Otto W. Yoerg.

MISSOURI

Annual Spring Clinic.—The St. Joseph Clinical Society will hold its seventh annual spring clinic at the Hotel Robideaux, St. Joseph, April 13-14. There will be no registration fee. The speakers will include:

Dr. James O'Donoghue, St. Joseph, Advances in X-Ray and Radium Therapy.
Dr. Vincil Rogers Deakin, St. Louis, Treatment of Acidosis in Renal Insufficiency.
Dr. Robert D. Alexander, St. Louis, Cancer of the Colon and Rectum.
Dr. Ernest Sachs, St. Louis, Brain Tumor.
Dr. Ralph V. Byrne, St. Joseph, New Clinical and Laboratory Concepts of Hyperthyroidism.
Dr. Thomas L. Howden, St. Joseph, Hypertension of the Menopause.
Dr. Robert S. Minton, St. Joseph, Eye Injuries.
Dr. Thomas G. Orr, Kansas City, Cancer of the Breast.
Dr. Rollin Russell Best, Omaha, Advances in the Treatment of Biliary Tract Disease.
Dr. Warren H. Cole, Chicago, Intestinal Obstruction.
Dr. Horace M. Korns, Iowa City, Diagnosis and Treatment of Peripheral Vascular Disease.
Dr. Henry H. Turner, Oklahoma City, Okla., Diagnosis and Treatment of Endocrine Disorders.

At the luncheon the first day Dr. Sachs will show a "Travelogue to Guatemala." In the evening a joint dinner meeting will be held with the Buchanan County Medical Society with Drs. Hugo Ehrenfest, St. Louis, and Clifford G. Grulee, Evanston, Ill., as the speakers on "Birth Injuries" and "Intracranial Hemorrhage of the Newborn" respectively. At a dinner the following evening Dr. Cole will speak on "Pancreatitis."

NEBRASKA

Society News.—Dr. Sanford R. Gifford, Chicago, was the guest speaker before the Omaha-Douglas County Medical Society, Omaha, February 8, on "Recent Advances in Ophthalmology." Dr. Joseph D. McCarthy, Omaha, discussed "Questionable Cholecystitis—Cholecystectomy and Its Aftermath" and Dr. Charles McMartin reported a case of vulvar verruca acuminata.——Drs. Edward H. Hashinger and Ferdinand C. Helwig, Kansas City, Mo., addressed the Lancaster County Medical Society, Lincoln, February 1, on "Various Phases of Obesity with Particular Emphasis on Endocrine Therapy" and "The Diagnostic and Therapeutic Importance of Endocrine Activity in Neoplastic Disease" respectively.——Drs. Warren Thompson and Joseph D. McCarthy, Omaha, addressed the Madison Six County Medical Society, Norfolk, January 18, on heart disease.

NEW YORK

Society News.—Dr. William Hadden Irish, New York, addressed the Westchester County Medical Society, White Plains, March 15, on "Common Disabilities of the Knee Joint."——Dr. William F. Rienhoff, Baltimore, addressed the Medical Society of the County of Albany March 23 on "Diagnosis and Treatment of Carcinoma of the Lung and Allied Conditions Such as Bronchiectasis and Pulmonary Abscess."

Cruising X-Ray Laboratory for Silicosis Tests.—The New York State Department of Labor has fitted a traveling x-ray laboratory to be sent to industrial centers where dust hazards are known or suspected to exist, the *New York State Journal of Medicine* reports. The traveling laboratory is 17 feet 9 inches long and 7 feet 4 inches wide. The rear half contains a reception and examining room, the other half the lead lined x-ray room.

Outbreak of Septic Sore Throat.—An outbreak of septic sore throat involving 300 cases with two deaths up to February 26 was reported to the state department of health recently from Norwood, a village in St. Lawrence County. Of 180 patients seen during an investigation, 87 per cent had used raw milk from a single dairy. A milker on the dairy farm became ill with sore throat January 28 and later two cows were found to have acute mastitis. The milk was pasteurized and no new cases were reported up to March 7, *Health News* stated.

New York City

Gifts to New York University.—The following are among the largest in a list of gifts to New York University for research in medicine:

Mrs. George B. deLong, $10,000 for the department of pediatrics.
The Commonwealth Fund, $8,750 for research in obstetrics and gynecology.
Lucius N. Littauer, $4,000 for studies on pneumonia.
Phi Delta Epsilon fraternity, $2,200 to establish the John Wyckoff Lectureship Fund.
Rockefeller Foundation, $3,500 for research in cellular physiology.
Committee for the Study of Suicide, Inc., $3,250 for study of suicide by the department of psychiatry at Bellevue Hospital.
Friedsam Foundation Inc., $1,800 for the Child Neurology Research Fund.
International Cancer Research Foundation, $1,500 for research in cancer.

Personal.—Drs. Charles McDowell, emeritus professor of physiology, and Orlando S. Ritch, a trustee of New York Medical College and Flower Hospital, were entertained at a luncheon March 9 in honor of the sixtieth anniversary of their graduation from the college.——Dr. Francis Peyton Rous of the Rockefeller Institute for Medical Research has been elected a corresponding member of the Academy of Sciences, Paris, in the division of the biologic sciences.

Dr. Jelliffe Honored.—Friends of Dr. Smith Ely Jelliffe have arranged a celebration of his thirty-fifth anniversary as editor of the *Journal of Nervous and Mental Disease*, to be held at the New York Academy of Medicine April 22. A symposium on neuropsychiatry will be presented at an afternoon meeting with the following program:

Dr. Earl D. Bond, Philadelphia, Balance in Psychiatric Research.
Dr. George Draper, New York, The Man Factor in Disease.
Dr. Frederick Tilney, New York, New Interpretation of the Hippocampus.
Dr. Oskar Diethelm, New York, Psychiatry and Neurology in the Last Fifty Years.
Dr. Karl A. Menninger, Topeka, Kan., Somatic Correlations with the Unconscious Repudiation of Femininity in Women.

Dr. Adolf Meyer, Baltimore, will open the program and Dr. Jelliffe will preside. In the evening there will be a dinner at which the following speakers will pay tribute to Dr. Jelliffe: Drs. Abraham A. Brill, Louis Casamajor, Henry Alsop Riley, all of New York, and Richard H. Hutchings, Utica. Dr. Foster Kennedy will be toastmaster.

OHIO

Northern Tri-State Meeting.—The annual meeting of the Northern Tri-State Medical Association will be held in Findlay April 12. Among the speakers will be:

Dr. Warren H. Cole, Chicago, Hyperthyroidism.
Dr. Max Thorek, Chicago, Electrosurgical Obliteration of the Gallbladder.
Dr. Irving S. Cutter, Chicago, Therapeutics of Later Years of Life.
Dr. Gilbert J. Thomas, Minneapolis, Infections Other Than Tuberculosis of the Urinary Tract.
Dr. James S. Speed, Memphis, Tenn., Central Fractures of the Neck of the Femur.
Dr. Max Cutler, Chicago, Indications and Limitations of Radiation in the Treatment of Cancer.
Dr. Alan Brown, Toronto, Some Common Disturbances in Children Frequently Handled Incorrectly.

Medical Library Association.—Dr. Carl H. Lenhart was elected president of the Cleveland Medical Library Association at its annual meeting in January. Dr. Lenhart has been directing librarian of the association for eighteen years. Dr. Clyde L. Cummer, chairman of the board of trustees, reported that the association now has assets amounting to about $400,000 in addition to the Allen Memorial Library building adjoining Western Reserve University. It has 52,000 volumes and receives 434 medical journals. During the past year 10,000 visits to the library were recorded; only 3,000 were visits from members, the remainder being from students and the general public. A portrait of the late Dr. Alfred A. Jenkins, president of the library association at his death Nov. 19, 1937, was presented on behalf of his family.

PENNSYLVANIA

Hospital News.—Ground was broken March 8 for the new Montgomery Hospital, Norristown, the cost of which is estimated at $525,000.——The Greene County Memorial Hospital was recently opened in Waynesburg. It has a capacity of seventy beds and cost $125,000, of which $70,000 was a loan from the federal government, $30,000 was appropriated by the county and $25,000 was raised by public subscription.

Society News.—Dr. Hobart A. Reimann, Philadelphia, addressed the Lycoming County Medical Society, Williamsport, March 11, on "Recent Advances in the Treatment of Certain Infectious Diseases."——Dr. George J. Kastlin, Pittsburgh, addressed the McKean County Medical Society, Bradford, January 18, on pneumonia control.——An obstetric and pediatric institute was presented at a meeting of the Westmoreland County Medical Society at the Mountain View Hotel near Greensburg, March 22, under the auspices of the state medical society. The speakers, all of Pittsburgh, were Drs. David Benjamin Martinez, William Paul Dodds, Charles J. Barone, William W. Briant Jr., Henry T. Price and David H. Boyd.

Philadelphia

Medical College News.—The Woman's Medical College of Pennsylvania celebrated its eighty-eighth anniversary, March 11. Dr. Martha L. Bailey, Dillsburg, presided and the speakers were Drs. Lida Stewart Cogill, Philadelphia, Kate Campbell Hurd Mead, Haddam, Conn., and Henry D. Jump.

Society News.—Speakers at a meeting of the Physiological Society of Philadelphia, February 21, included Drs. Dale R. Coman, on "The Effect of Sulfanilamide on Chemotropism of Leukocytes," and Paul E. Adolph and John S. Lockwood, "The Use of Sulfanilamide in Experimental Hemolytic Streptococcal Meningitis."——Dr. Ward J. MacNeal, New York, addressed the Eastern Pennsylvania Chapter of the Society of American Bacteriologists, February 22, on "Bacteriological Service in Septic Conditions."——A program of ten minute papers on cancer was presented at a meeting of the Philadelphia County Medical Society, March 9, by the following physicians: Drs. Ralph S. Bromer, Bryn Mawr; Willard S. Hastings, Sigmund S. Greenbaum, George M. Dorrance, Howard H. Bradshaw, William Bates, William H. MacKinney, Dorothy C. Blechschmidt and William Wayne Babcock. Dr. Maurice E. Binet, Vichy, France, addressed a special meeting of the society, February 25, on "Hepatic Insufficiency."

Pittsburgh

Pediatric Survey.—The Allegheny County Medical Society is sponsoring a pediatric survey for graduate physicians with no limit on the number permitted to register, the first of its type offered by the society in its twelve years of presenting graduate courses. Sessions were held at the Children's Hospital and Magee Hospital March 14 and 21, Allegheny General Hospital March 28; succeeding ones will be at the Pittsburgh Home for Babies, Watson Home for Crippled Children, Tuberculosis League, Municipal Hospital for Contagious Diseases and the Children's Hospital. Dr. Theodore O. Elterich is general chairman for the course.

Society News.—Dr. Max M. Peet, Ann Arbor, Mich., delivered the Stewart Memorial Lecture of the Pittsburgh Academy of Medicine, March 22, on "Treatment of Hypertension by the Subdiaphragmatic Resection of the Splanchnic Nerves."——Guest speakers at a meeting of the Allegheny County Medical Society, March 15, were Dr. Benjamin I. Golden, Elkins, W. Va., on "Present Day Status of the Inguinal Hernia, with Discussion of Its Recurrence" and Rabbi Solomon B. Freehof, Pittsburgh, on "The Citadel of American Medicine."——At a meeting of the Pittsburgh Surgical Society March 29 the speakers were Drs. Daniel P. Greenlee, on "Adenoma of Islets of Langerhans with Hyperinsulinism"; Otto C. Gaub, "Errors in Development of the Intestinal Tube Below the Stomach from the Surgical Standpoint," and Lyndon H. Landon, "The Surgical Problem of Gastric Ulcer."

TEXAS

Society News.—Dr. Paul C. Williams, Dallas, addressed the Grayson County Medical Society, Sherman, recently on "Lesions of the Lumbosacral Spine."——Drs. Nellins C. Smith, Hillsboro, and Otto G. Zacharias, Whitney, addressed the Hill County Medical Society, Hillsboro, recently on "Serum Treatment for Lobar Pneumonia" and "Sulfanilamide Therapy," respectively.——Drs. Louie E. Allday and Cecil O. Patterson, Dallas, addressed the Titus County Medical Society, Mount Pleasant, February 8, on "Therapy of Pneumonia with Especial Reference to the Various Serums Used" and "The Medical and Dietetic Management in Acute Cholecystitis" respectively.——Drs. Simeon H. Hulsey and William L. Howell, Fort Worth, addressed the Brown-Mills-San Saba Counties Medical Society, Brownwood, January 10, on "Bronchiectasis" and "Diagnosis of Heart Conditions" respectively.——Drs. Harold L. D. Kirkham and Edwin Ghent Graves, Houston, addressed the Jefferson County Medical Society, Port Arthur, January 10, on "Facial Injuries" and "Recent Advances in Internal Medicine" respectively.——Dr. Byron A. Jenkins, Lubbock, addressed the Lubbock-Crosby Counties Medical Society, Lubbock, January 4, on "The Infant's Diet During the First Year."——A symposium on sulfanilamide therapy was presented at a meeting of the Tarrant County Medical Society, Fort Worth, January 4, by Drs. Horace S. Renshaw, Douglas G. Mitchell, Craig W. Munter, Thomas H. Thomason and Sidney E. Stout, all of Fort Worth.

PHILIPPINE ISLANDS

Personal.—Dr. Eusebio D. Aguilar, Manila, has been appointed director of the bureau of public welfare for the islands.——Dr. Gregorio Lantin, Manila, has been made head of the medicolegal section of the department of justice.

University News.—The board of regents of the College of Medicine, University of the Philippines, recently abolished the medicolegal department of the school. Sixto de los Angeles, L.M., head of the department since its establishment, has resigned.

GENERAL

Scholarship in Psychiatry.—The Institute of International Education announces that a Woolley scholarship in Paris is offered to a student in psychiatry for the year beginning October 1. The scholarship consists of $600 and a room in the United States House of the Cité Universitaire in Paris, under whose auspices the offer is made. To qualify, a candidate must be an American citizen, hold a medical degree or be in the last year of study for it, be under 30 and unmarried and have a good working knowledge of the French language. For application blanks apply to the Institute of International Education, 2 West Forty-Fifth Street, New York.

Academy of Arts and Sciences to Award Septennial Prize.—Announcement is made of the "Francis Amory Septennial Prize" to be awarded by the American Academy of Arts and Sciences for "outstanding work with reference to the alleviation or cure of diseases affecting the human genital organs." The fund providing the award was a gift of the late Francis Amory, Beverly, Mass. It will amount to more than $10,000 and may be given in one or more awards, the first in 1940 if work of a quality to warrant it is presented. There will be no formal nominations, and no formal essays or treatises will be required. Suggestions should be made to the Amory Fund Committee, 28 Newbury Street, Boston.

New President of Parke, Davis & Company.—Dr. Alexander W. Lescohier, Grosse Pointe, Mich., was elected president of Parke, Davis & Company at a meeting of the board of directors in Detroit March 1, to succeed Oscar W. Smith, who died February 7. Dr. Lescohier has been general manager and a director since 1929. He joined the staff of Parke, Davis & Company in 1909, the year of his graduation from Detroit College of Medicine. In 1918 he was named assistant director of the research and biologic laboratories, where he was in charge of the production of serums, vaccines, antitoxins and other biologic products; in 1925 he was made director of the department of experimental medicine and in 1928 assistant to the president.

The Annual Golf Tournament in San Francisco.—The twenty-fourth annual tournament of the American Medical Golfing Association will be held at the San Francisco Golf and Country Club Monday June 13. The association has planned a tour for its members, beginning with an ocean trip from New York to New Orleans and including six games at cities on the way. The group will sail from New York June 1 and play its first game in New Orleans June 7. Games will be played at Houston, Galveston, San Antonio, Los Angeles and Del Monte, Calif. The return trip will be through Portland, Seattle, Vancouver, Lake Louise and Banff, with two more games and a trip up Puget Sound. The president of the association is Dr. Walt P. Conaway, 1723 Pacific Avenue, Atlantic City, N. J., and the executive secretary is Bill Burns, 2020 Olds Tower, Lansing, Mich.

Changes in Status of Licensure.—The North Dakota State Board of Medical Examiners recently reported the following action:

Dr. John Morgan Phillips, Bisbee, license suspended following charges of having performed an illegal operation.

Dr. Joseph Allaire, Olga, license suspended after his pleading guilty to use of narcotics.

The Commission on Licensure of the Medical Society of the District of Columbia announced the following:

Dr. James D. Eggleston, Takoma Park, Md., license revoked January 21, having been convicted of performing an illegal operation.

The Virginia State Board of Medical Examiners reports the following recent action:

Dr. Robert Clay Hogue, Richmond, license revoked, following his conviction of violation of the Harrison Narcotic Act.

The Illinois State Board of Registration and Education announces the following:

Dr. Benjamin McChapman, Chicago, license restored, Dec. 21, 1937.

Dedication of Indian Hospital.—Dr. William W. Peter, medical director of the Navajo-Hopi Indian Reservations in northeast Arizona, sends a special invitation to physicians attending the annual session of the American Medical Association in San Francisco June 13-17 to attend the dedication of a new base hospital for the reservation at Fort Defiance June 20. Three days of clinics will follow. Those who contemplate visiting the reservation for this occasion should write to Dr. Peter at Window Rock, Ariz., giving expected date of arrival, length of stay and number in party so that reservations can be made either at Gallup, N. M. (the nearest town, 31 miles from Fort Defiance) or in the dormitories at Fort Defiance. Tours over the 25,000 square mile reservation will be arranged on request. Physicians and public health workers in states bordering Arizona are also invited.

Foreign Letters

LONDON

(From Our Regular Correspondent)

March 5, 1938.

Yellow Blackboards

The National Institute of Industrial Psychology has turned aside from its investigations of the working conditions of factories and offices to those of schools and directed its attention to the strain of copying from the blackboard. It has now published an investigation entitled "Improving the Blackboard," by Dr. W. D. Seymour, which may render that time-honored article obsolete. The strain felt by children copying from the blackboard may be partly due to the repeated movements of the head and eyes and to changes of accommodation, but the question arose whether it was also due to copying from a black board on to white paper. The former has a reflection factor of from 10 to 15 per cent while the latter has one of from 85 to 90 per cent. The object of the investigation was to find whether a board with a much higher reflection factor than a black board would enable children to copy from it more quickly and with less strain. As a white board would cause glare, a light yellow board was chosen for the experiments, with blue as the color for the chalk. An instrument was devised to record on a moving tape the time taken by adults to read successively exposed short syllables presented first in white letters on a black board and then in dark blue letters on a yellow board. The words on the yellow board were read more quickly, the average difference being 15.4 per cent. The experiment was then made in the class room of getting children to copy the usual white letters on a black board and comparing the result with copying from a yellow board. The results showed an advantage in time of 10 per cent for the latter. It is suggested that this saving in time represents a material reduction in strain. A further investigation is being made of the most suitable material from which boards of the color found best from the visual standpoint may be constructed.

Medicine and Eugenics

In his Galton lecture to the Eugenics Society, Prof. J. A. Ryle made a plea for greater attention to eugenics. Planning for national health and efficiency should be in the hands of the three great applied sciences—medicine, eugenics and sociology. Medicine, he regretted to say, was so taken up with urgent practical affairs that it had scarcely found time to consider what its true objectives are. Between the three there was at present no true cooperation. It was rare to meet among physicians one with even the rudiments of genetics or more than a superficial interest in the prospect of race betterment by eugenic education or legislation. The Eugenics Society had 650 members, only one fifth of whom were physicians. The membership should be much higher and the proportion of physicians should be increased if any large and effective policy was to come forth. A program to solicit the fuller cooperation of medicine would be more effective than any propaganda to awaken interest in lay audiences. Professor Ryle made the following practical recommendations:

1. A national council should be formed embodying the triple alliance between medicine, eugenics and sociology, with representatives in each instance of the academic and applied sciences and appropriate contacts with the ministries and research departments of health, agriculture and labor. This council should be advisory for education, research in human genetics and social reorganization. It should regularly transmit to the legislative councils of the country the information accumulated, with suggestions for reform based thereon. In the preventive field such a council might stand in the same relation to the government as the Medical Research Council now stands for the problems of medical research and its application to practice.

2. As part of a general reform in medical education, the curriculum should be modified to lay more stress on all preventive aspects. The preservation of health by nutritional and other social reforms and by applications of human and animal genetic studies to eugenic education and legislation should receive fuller emphasis, both in the preclinical and in the clinical periods. In the clinical period, teachers should recognize a special duty in connection with the prophylactic aspects of medicine.

3. With the help of existing organizations, eugenic and sociologic, an endeavor should be made to interest the physicians of the country, through their medical and scientific societies, in the preventive and educational role which they might themselves fulfil by instruction in domestic eugenics, both positive and negative. The preservation of health as a primary function, with the treatment of disease as a secondary function, should become the new ideal.

4. A limited number of research chairs or readerships in human genetics should be established, preferably in universities where the medical and biologic services already function side by side.

An Australian Premarriage Clinic

A premarriage clinic has been opened in Sydney, where health tests are available for couples about to marry. The clinic is subsidized by the state government of New South Wales and is sponsored by the Racial Hygiene Association. It arranges an exhaustive overhaul by any of twelve specialists for a nominal fee. It issues certificates that (1) the parties contemplating marriage are fit to marry and raise a family, (2) the marriage should be delayed for from three to six months or (3) the marriage should be permitted without parentage or should be discouraged. The clinic receives letters from young people on marriage problems at the rate of 100 a month.

Sir Thomas Stanton

Sir Thomas Stanton, chief medical adviser to the secretary of state for the colonies and co-discoverer of the cause of beriberi and a pioneer worker on other tropical diseases, has died in London. Born in Canada in 1875, he graduated M.D. from Toronto and continued his medical studies in London at University College Hospital and the London Hospital. At the Hospital for Tropical Diseases he became house surgeon to Manson, who appointed him demonstrator. In 1907 he went to the Malay States to assist Henry Fraser, director of medical research at Kuala Lumpur, in an attempt to discover the cause of beriberi. They experimented with two groups of coolies who were making a road through virgin jungle. One group was fed on polished rice, the other on parboiled rice. They were thus able to prove that beriberi was due to feeding on rice from which the outer layers had been removed by polishing. They found that the subpericarpal layers contained certain "alcohol-soluble substances minute in amount but of high physiological value in nutrition." Thus the important new conception of "a deficiency disease" entered medicine. It was not until some years later that Funk introduced the name vitamin for such substances. Stanton and Fraser wrote numerous valuable papers on beriberi, which were republished in a volume entitled "Collected Papers on Beriberi." He was able to write in the preface: "Beriberi, which was formerly a scourge in the Orient, is now well on the way to extinction." Stanton was also an excellent entomologist and did work on the identification of mosquito larvae almost as important as that on beriberi. He also discovered that an obscure and fatal disease which appeared in 1917 among the laborers on rubber estates was due to an organism like that of glanders. He named the disease "melioidosis."

PARIS

(From Our Regular Correspondent)

March 5, 1938.

Cevitamic Acid in the Treatment of Addison's Disease

Few reports have appeared on the use of cevitamic acid in Addison's disease, although the results of the research of Szent-Györgyi justify such a treatment. At the January 21 meeting of the Société médicale des hôpitaux a case was reported by Laederich and his associates in which gratifying results followed the use of cevitamic acid in Addison's disease. The patient was a male nurse, aged 31, whose chief complaints on admission to the hospital, Sept. 9, 1937, were severe asthenia and gastrointestinal disturbances of six months' duration. Examination revealed the typical skin pigmentation found in Addison's disease, especially marked on parts of the body exposed to the air as well as on the buccal mucosa. The asthenia and emaciation were also apparent. The epidermal reaction to tuberculin was markedly positive. The Wassermann reaction was negative. Until October 11 a daily hypodermic injection was given of adrenal cortex extract but the patient's condition showed no improvement. Cevitamic acid was then given in doses of 1 Gm. daily in a single dose. Within ninety-six hours after this treatment was begun, i. e., as soon as the acid appeared in the urine, a striking improvement was noted in the form of cessation of emesis and diarrhea with return of appetite. The patient was able to get out of bed October 20 and the skin and mouth pigmentation began to lessen until the middle of November, since which time it has remained stationary.

Harris, Ray and Ward have called attention to the fact that delay in the appearance of cevitamic acid in the urine of patients suffering from vitamin C subnutrition is an excellent way of evaluating the degree of avitaminosis. This method was applied in the case reported by Laederich and his associates. In spite of the administration of 3.6 Gm. of cevitamic acid during the first four days, none of the acid was found in the urine. Similar observations in five cases of Addison's disease have been reported by others. The rapid disappearance of the asthenia, digestive disorders and genital disturbances as in the present case has not been reported previously. The authors consider their case as symptomatically improved following the use of cevitamic acid in large doses.

Diagnostic Centers for Low-Income Classes

To avoid the conversion of the medical profession into government officials in the state's effort to socialize medicine, the secretary of the organization which looks after public relations for the profession here proposed about a year ago to establish diagnostic centers all over France. These centers were to be organized by what corresponds to the county medical societies in the United States. The staffs were to be composed of the specialists and general practitioners of each county. The chief objective of each center was to be preventive medicine, in the form of examination of patients referred by local practitioners whose income did not permit payment of the laboratory and specialist fees incidental to the diagnosis of conditions difficult to recognize with the facilities usually at the disposal of the general practitioner. This idea of diagnostic centers was the subject of much discussion at the annual meeting in December 1937 of the Confédération des syndicats médicaux, delegates from all of the ninety departments of France taking part. Only one county society had tried such a diagnostic center plan. The secretary of this society reported that quarters had been placed at their disposal by the county hospital. Patients in the low-income class are sent by their attending physicians with a slip indicating that certain examinations ought to be made, some of which might require the services of specialists. Following a complete study of a given case, the patient is sent back to his physician with the results of the various examinations. No effort is made to treat those in the low-income class; this is carried out only in the case of indigents, for whose care the county authorities pay. Those in the low-income class are charged a fee merely sufficient to pay for laboratory charges.

The Antituberculosis Campaign

Prof. Fernand Bezançon read a paper at the February 22 meeting of the Académie de médecine of Paris in which he showed how differently pulmonary tuberculosis is regarded at present from what it was twenty years ago. At that period it was believed that the appearance of the disease in adult life was simply a recrudescence of a primary infection in infancy, and hence the objectives of the fight against tuberculosis were to isolate children from possible contagion and to attempt to eliminate any cause which could favor its lighting up in adults. The Pirquet test appeared to show that the number of positive reactions increased with age until they attained 97 per cent in adults. Recent contributions to the subject by American and northern European phthisiologists, confirmed in France, have shown that the statistics of an almost universal positive reaction in adults were based on dispensary observations made among the poorer classes and that in reality if one applies the tuberculin test to those residing but a short time in the larger cities as well as to those in the middle and upper classes of society it would be found that from 30 to 40 per cent of young adults showed a negative reaction. Hence the question arises as to whether a large number of the tuberculous manifestations seen in adolescents and young adults ought not to be considered late primary infections rather than a lighting up of a primary infection in nurslings and young children. It follows that exposure to infection in adults plays a far more important part than any other cause; hence the lesson to be drawn from the observations of Scandinavian phthisiologists is that under no conditions should persons who have a negative tuberculin reaction be permitted to do any work in which they are exposed to contact with tuberculous persons. This applies particularly to medical students and pupil nurses.

Another question is whether it is necessary to separate children showing a positive tuberculin reaction from contact with tuberculous parents. The recent observations of Professor Bezançon and his co-workers (Negative Tuberculin Skin Reactions in Children, THE JOURNAL, Oct. 16, 1937, p. 1289) have shown that children exposed to such infection by parents have either curable forms of the disease or only a positive skin reaction or present no evidences of infection.

One of the most important tasks for those interested in the subject, in the near future, is to follow individuals showing either positive or negative reactions when exposed to tuberculous infection.

Early diagnosis not only with the aid of the skin reactions but also by means of radiography and thorough clinical examination is the immediate goal of the fight against tuberculosis. The dispensary must remain the keystone of the arch in this fight, aided by the work of visiting nurses who will supervise home hygiene. The sanatorium ought to become more and more an active treatment center and not to be filled up with patients who really do not need sanatorium care, such as those recovering from a hemoptysis without bacilli in the expectoration, and only discrete radiologic evidence of disease. Also to be excluded are those convalescing from pleurisy; also old fibrous tuberculosis patients and those with chronic bronchitis and emphysema. For the first named preventoriums or convalescent homes should be created. The more chronic cases should be cared for in special hospitals for this purpose. The sanatorium should be reserved for cases in active evolution and these patients

should be sent home as soon as the acute stage has passed. Tuberculosis causes more than 60,000 deaths every year in France, and between 500,000 and 600,000 persons here have the disease.

BERLIN

(From Our Regular Correspondent)

Feb. 14, 1938.

Investigation of Blood Donors

Dr. K. A. Seggel of the Leipzig Medical Society investigated the blood donors of his city. The total number of recorded requests for blood donors was 1,865. Thorough preliminary and subsequent observation of the donor is an urgent necessity; it should include complete serologic examination. In all, 1,042 such examinations were carried out. The total amount of blood donated was 672 liters. The number of donors varied, 195 blood donors' certificates being issued; thirty-two donors had undergone more than twenty transfusions and eight more than thirty. The maximum per donor was thirty-three transfusions. There were forty-five donors who had provided more than 6 liters of blood, ten of whom had given in excess of 10 liters; the maximum was 12 liters. Good medical care of the donor is certainly desirable, since frequently a substitute is difficult to find. There is a steadily increasing demand for blood donors. Formerly only forty-seven transfusions were performed in a quarter; now the number is around 240. The national ministry of the interior regulates the compensation of donors.

Disturbances due to incorrect blood typing of recipients are avoidable; two cases were reported in each of which 400 cc. of atypical "incompatible" blood was transfused without untoward clinical consequences. On the contrary, in five cases transfusions of smaller amounts (from 10 to 375 cc.) of atypical "incompatible" blood were followed by disturbances: hemolysis, nephritis, and so on. The so-called Oehlecker biologic preliminary test is considered distinctly unreliable. In one case mild clinical symptoms followed transfusion of O blood to an A recipient whose blood had incorrectly been typed as O. Thus far it has been impossible to avoid occasional disturbances even if the blood of donor and recipient is compatible on the basis of the classic fourfold grouping; especially noteworthy incidents in point were four cases of icterus (three of the patients were of group A, one of group AB) and three cases of hemoglobinuria all in group A patients. The majority of recipients in the mentioned cases had tolerated without any incident other transfusions of similar type blood both previously and subsequently. One is surprised to find that these anomalous cases always concerned a recipient of the A type; possibly these phenomena indicate that persons of A_1 type may present an α_2 and persons of A_2 type an α_1. Such incidents are, however, extremely rare (seven instances; in all, 1,865 transfusions). Prophylaxis by exact evaluation of the peculiarities of the subgroups is virtually impossible in clinical practice.

Improved Cardiac Diagnosis

Prof. A. Weber, Nauheim cardiologist, recently lectured to the Frankfort Medical Society on improved cardiac diagnosis. He called particular attention to four diagnostic technics:

1. Evaluation of arterial sounds by auscultatory measurement of blood pressure. By the quality of these sounds the magnitude of the cardiac output may be gaged. Arterial sounds are always more distinct under circumstances in which increased cardiac output would be expected: after physical exercise, in states of psychic excitation, in aortic insufficiency, after an extrasystole with prolonged compensatory pause and in feverish patients whose hearts are healthy. Subdued arterial sounds are heard under other conditions; e. g., in aortal and mitral stenoses, in collapse and in coronary thrombosis. Intermittent loud and soft arterial sounds accompany the pulsus alternans. A diminution of the arterial sounds in the febrile stage of infectious disease or in narcoses is an earlier portent of circulatory failure than a fall in blood pressure.

2. Evaluation of the venous pulse. Systemic circulatory stasis leads to premature termination of the systole, a symptom usually present in mitral stenosis. Enlargement of the presystolic waves and simultaneously appearing small systolic waves are also characteristic for mitral stenosis. The manifestation of an "insufficiency wave" which rises with the beginning of the first sound, and which therefore precedes the systolic venous wave, indicates tricuspid insufficiency.

3. Evaluation of the heart sounds. A graphic record of the heart sound curve obtained with proper apparatus represents an objective check on the data elicited by auscultation. Moreover, the heart sound curve provides a whole group of data imperceptible to the most expert auscultatory technics. An example in point would be the soft abnormal sound phenomena that sometimes accompany intense audible sounds. From auscultation one obtains a decidedly incomplete impression of the duration of a sound. In coronary sclerosis, hypertension and so on, highly significant signs such as presystolic murmurs are imperceptible by auscultation. Yet this type of bruit is actually common and is an objective indication of left ventricular failure. Supernumerary sounds, often detected with difficulty by auscultation, nearly always become plainly demonstrable in a correct recording of the heart sounds.

4. Electrocardiography, the technic by which various arrhythmias are evaluated and the diagnostic aid *par excellence* in coronary disease and myocardial lesions both ephemeral and chronic.

The Heritability of Neuropathic Muscular Atrophy

Formerly the term neural muscular atrophy was applied to those forms of progressive muscular atrophy in which the peripheral nerves as well as the musculature undergo degeneration while the cells of the anterior horn of the spinal cord present only insignificant changes, or no changes whatever. But as H. Boeters stated in a lecture before the German Society of Genetics, the degeneration of the peripheral nervous system is not a uniformly present condition, whereas degenerative changes in the cells of the anterior horn and atrophy of the anterior root are always demonstrable. The clinical picture varies in correspondence with the progress of the degenerative processes objectively observed. The disease usually begins in the first or second decade of life and is characterized by a slowly progressive muscle atrophy which attacks various parts of the extremities, especially the calf of the leg. Areflexia, vasomotor disturbances and changes in response to electrical stimuli are also present. In addition to the peripheral changes, some cases are marked by degenerative changes in the gray columns (these cases develop into Friedreich's ataxia). In still other cases, changes in the lateral pyramidal columns are observed. In view of these variations "neural muscular atrophy," a designation that implies a limitation of the process to the peripheral venous system, can no longer be considered correct.

The hereditary transmission of the disorder has not been well understood. Boeters therefore recently undertook pertinent investigation of a total of 1,128 persons in thirty-five different families. In addition to the original forty-two cases of neuropathic muscular atrophy, which led to the selection of the families studied, Boeters discovered 121 other cases among relatives. In a large majority of cases the disease had been directly transmitted from parents to children over several generations. In a small number of instances the disorder was present in siblings but the parents were healthy. Close investigation of these allegedly "healthy" parents, however, often elicited histories of relatively mild anomalies: talipes cavus, slight atrophy of the musculature of the calf accompanied by

areflexia, complaints of weakness and apparent crippling of a leg on exposure to cold. The foregoing observations indicate that the disease most often is not strongly manifested and the predisposition may accordingly be wholly checked. Still there may persist an (incomplete) dominant transmission coexistent with a relatively slight penetration and active expression of the trait. This observation is corroborated by the morbidity statistics. In the material studied by Boeters the ratio of males affected by neuropathic muscular atrophy to females similarly affected was 2:1 (a ratio in agreement with other data). A sound interpretation of this variation has yet to be made. Besides, it is still problematic whether the female sex exerts an inhibitory influence on the manifestation or whether men as a consequence of stronger demands made on them; namely, more marked environmental influence, are more frequently the victims. In Boeters' material the onset of the disorder lay between the sixth and the twentieth year of life. Great variability was noted with respect to the course and severity of the disease. In fact, certain families presented pluralities of cases so similar, even to minute characteristics, that a sort of familial type of the disease was considered probable. The social value of the patients was extremely diverse. Families in which the disorder was manifested preponderantly or exclusively in a milder form were rare. If the disease began early and progressed the patient did not procreate; on the contrary, a late inception and mild course of the disease did not prevent marriage and procreation. The general course of the atrophy is severe and in Boeters' opinion justifies sterilization of the sufferer, provision for which is made in the German law.

NETHERLANDS

(From Our Regular Correspondent)

Jan. 25, 1938.

Plumbism Among Cigar Makers

Following the official report of forty-one cases listed as lead poisoning among the employees of fourteen cigar factories in the southern part of the country, an inquiry was inaugurated by the medical service of the factory inspection bureau. More than half of these cases and other cases subsequently reported were characterized by gingival lines. There were also a number of suspected cases. The inquiry was principally concerned with the underlying cause of these accidents. Three possible sources of contamination were considered: (1) the sheets of zinc on which the cigars are cut (cf. Pel's case, *Zentralbl. f. inn. Med.* **18**:545, 1897), (2) the factory drinking water and (3) the drinking water in the homes of workers affected. A combination of these sources was thought to underlie some cases. The respective importance of the mentioned factors was regarded as unequal; the water, which in many instances was pumped from wells, was considered of greater significance than the zinc sheets. The health authorities have advised the various community governments and the public at large that for the time being there ought to be a revival of the old well bucket or at least a rejection of the first water to issue from the pump. This first flow of water, so commonly used in preparation of the morning coffee, probably will have stood all night in the leaden pipe.

Care of the Babies of Unmarried Mothers

Dr. Knapper investigated the type of care received at present by the babies of unmarried mothers in the Netherlands. One organization, the Federation of Maternity Homes for the Unmarried Mother, is exclusively devoted to this problem. There are forty-seven such institutions under public control and many others under private auspices. Knapper concluded from his observations that the problem is far from being satisfactorily solved. The author places special emphasis on the following conditions which call for amelioration: buildings often antiquated, crowded and poorly ventilated; financial resources insufficient to permit the mothers to suckle their babies during the first three months; poorly trained nursing personnel; unhygienic conditions that inevitably breed epidemics. Dr. Knapper suggests that proper care of the unmarried mother ought to be assured by law.

Tuberculosis Mortality in the Netherland East Indies

Whereas, according to official statistics of the Netherland Indies, the mortality from paludism was only 5 per cent, that of typhoid 4 per cent, that of dysentery 3.5 per cent and that of cancer 3 per cent, the death rate from tuberculosis was 13.5 per cent. The last named disease thus claims more victims than all the other mentioned maladies together. It is important therefore to determine which elements of the population are chiefly affected by tuberculosis.

Data from the Tuberculosis Center at Surabaya and the sanatorium at Batoe indicate an equal morbidity from the disease in all elements of the population. At the Surabaya center 1,534 patients were examined in the year 1916; of these, 75 per cent were native, 15 per cent Chinese and 10 per cent European. Of a similar clinical material at the Batoe sanatorium 47 per cent were native, 34 per cent Chinese and 19 per cent European. If one considers that the average native is loath to visit a center and *a fortiori* to be hospitalized, it follows that the morbidity from tuberculosis among the indigenous population must be extremely high.

Queen Wilhelmina Institute of Leprosy Research

The Queen Wilhelmina Institute, although it treats leprous patients in its hospital wards and dispensary, is primarily a research institution. The plant is divided into two sections: in the first are housed the laboratories, the experimental animals, the services of photomicrography and photomacrography, the library and so on; the second section contains the hospital wards (which are carefully arranged in accordance with the studies to be made and treatment to be administered) and the isolation units. The institute is directed by Dr. Lampe. Associated with him is Dr. Lobel, bacteriologist and veterinary. Here, for the first time in the history of leprosy research, veterinary medicine forms an integral part of the medical-scientific approach.

At the first Netherland Indies Congress on Leprosy, many papers were read and discussed. The committee stressed the importance of the problem in question and announced that similar congresses would be held at regular intervals in the future.

Marriages

ELBERT ALEXANDER MACMILLAN, Winston-Salem, N. C., to Miss Nora Irene Frantz of Clymer, Pa., in Philadelphia, Dec. 6, 1937.

J. PHELPS HAND JR., Washington, D. C., to Miss Lida Lee Gregg of Manchester, Ga., in Baltimore, Dec. 29, 1937.

DAVID WALLACE MACKENZIE JR., New York, to Miss Kathlyn Byers of Fort William, Ont., Canada, in February.

CHARLES G. HILL, Philadelphia, to Miss Caroline Catherine Stump of Irwin, Pa., Dec. 24, 1937.

JOSEPH J. MILLER, Pittston, Pa., to Miss Helen Corlyn Ross of Wilkes-Barre, Dec. 16, 1937.

ROLAND P. WILDER to Miss Dorothy E. Reeves, both of Malden, Mass., Oct. 27, 1937.

PAUL L. WOLPERT, Onawa, Iowa, to Miss Katherine Block of Sioux City, February 10.

JOSEPH F. ROTH to Miss Belva Gibbons, both of Wilkes-Barre, Pa., Dec. 13, 1937.

GEORGE D. OLIVER, Quesnel, B. C., to Miss Louise Clunness, Dec. 2, 1937.

Deaths

Michael Anthony Burns ✠ Philadelphia; Jefferson Medical College of Philadelphia, 1907; professor of neurology since 1934 at his alma mater, and served successively as demonstrator, lecturer, associate, assistant professor and associate professor; visiting neurologist to the Philadelphia General Hospital, neuropsychiatrist to St. Mary's Hospital, consulting physician to the Institute for Mental Hygiene of the Pennsylvania Hospital, consultant neurologist to St. Joseph's Hospital and attending neurologist to Jefferson Hosptal; served during the World War; aged 53; died, March 7, of heart disease.

Thomas Herbert Patton, Tuscaloosa, Ala.; Tulane University of Louisiana Medical Department, New Orleans, 1912; member of the Medical Association of the State of Alabama; fellow of the American College of Surgeons; aged 53; on the staffs of the Veterans Administration Facility and the Druid City Hospital, where he died, January 19, as the result of injuries received in a fall from a window.

Sherman McKenney, Fremont, Ohio; Detroit College of Medicine, 1892; served during the World War; formerly county coroner and county health officer and member of the school board; on the staffs of the Community Hospital and the Memorial Hospital; aged 70; died, January 16, of coronary occlusion, while aboard the S. S. *Mariposa,* en route to San Pedro, Calif., on a cruise to Australia.

George H. Penrose, Col., Q. M. C., U. S. Army, Washington, D. C.; University of Buffalo School of Medicine, 1886; veteran of the Spanish-American War; served in the quartermaster corps of the army in various capacities; in 1920 was made a colonel, and retired in 1922 at his own request after twenty-four years' service; aged 76; died, January 6, in the Walter Reed General Hospital.

Luther Hess Hamilton ✠ Portland, Ore.; Jefferson Medical College of Philadelphia, 1901; member of the North Pacific Surgical Association; fellow of the American College of Surgeons; at one time assistant clinical professor of surgery at the University of Oregon Medical School; on the staff of the Good Samaritan Hospital; aged 64; died, January 16, of cerebral hemorrhage.

James A. Pickett, El Paso, Texas; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; member of the State Medical Association of Texas; past president of the El Paso County Medical Society; on the staffs of the City-County Hospital and the Hotel Dieu, Sisters Hospital; aged 55; died, January 27, of peritonitis following an operation.

Hermann Feit ✠ New York; Rheinische Friedrich-Wilhelms-Universität Medizinische Fakultät, Bonn, Prussia, 1919; dermatologist to the Vanderbilt Clinic, Columbia University, Englewood (N. J.) Hospital, Greenville Hospital, Jersey City and the New York Skin and Cancer Hospital; aged 47; died, January 18, of a malignant growth.

William August Engsberg, Lakemills, Wis.; Rush Medical College, Chicago, 1891; member of the State Medical Society of Wisconsin; at one time mayor of Lakemills; bank president; aged 70; died, January 18, in the Madison (Wis.) General Hospital, of pulmonary embolism and hypertrophy of the prostate.

John Walker Hauxhurst, Bay City, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1876; member of the Michigan State Medical Society; past president of the Bay County Medical Society; on the staff of the Mercy Hospital; aged 89; died, January 22, of cerebral hemorrhage.

Bradley A. Fowler, Brownwood, Texas; Vanderbilt University School of Medicine, Nashville, Tenn., 1888; member of the State Medical Association of Texas; formerly on the staffs of the Medical Arts Hospital and the Stump General Hospital; aged 72; died, January 29, of coronary thrombosis.

Russell Park Glenn, Abilene, Texas; Atlanta College of Physicians and Surgeons, 1905; fellow of the American College of Surgeons; on the staff of the West Texas Baptist Sanitarium; member of the State Medical Association of Texas; aged 64; died, January 2, of coronary occlusion.

Marie Louise Chard ✠ New York; Woman's Medical College of the New York Infirmary for Women and Children, New York, 1895; fellow of the American College of Surgeons; on the staff of the New York Infirmary for Women and Children; aged 70; died, January 20, of myocarditis.

Frank L. Magoon, St. Louis; St. Louis College of Physicians and Surgeons, 1892; member of the Missouri State Medical Association; past president of the board of education, and formerly vice president of the board of police commissioners; aged 70; died, January 17, of heart disease.

Mary Bunker Jepson ✠ Olean, N. Y.; Hering Medical College, Chicago, 1895; past president of the Cattaraugus County Medical Society; on the staff of the Olean General Hospital; aged 70; died, January 2, in Miami Beach, Fla., of chronic lymphatic leukemia.

Peter D. Bixel ✠ Pandora, Ohio; Eclectic Medical Institute, Cincinnati, 1901; formerly county coroner; president of the county board of health; on the staff of the Bluffton (Ohio) Community Hospital; aged 72; died suddenly, January 2, of coronary thrombosis.

Pierre Hoa Le Blanc, New Orleans; Tulane University of Louisiana Medical Department, New Orleans, 1894; medical examiner for the Life Insurance Company of Virginia; aged 69; died, January 4, of chronic myocarditis and coronary thrombosis.

John Elmer Hammer, Kiowa, Kan.; University Medical College of Kansas City, Mo., 1913; member of the Kansas Medical Society; served during the World War; aged 48; died, January 2, in a hospital at Wichita, of auricular fibrillation.

Lachlan MacLean Beatson ✠ Arkansas City, Kan.; University College of Medicine, Richmond, Va., 1908; served during the World War; for many years member of the board of education; aged 54; died, January 2, of angina pectoris.

Andrew J. Crawford, Glouster, Ohio; College of Physicians and Surgeons, Baltimore, 1887; member of the Ohio State Medical Association; formerly member of the state legislature; aged 75; died, January 11, of arteriosclerosis.

Carl James Emmerling ✠ Pekin, Ill.; University of Illinois College of Medicine, Chicago, 1926; on the staff of the Pekin Public Hospital; aged 37; died, January 23, in the Proctor Hospital, Peoria, of carcinoma of the lung.

Joseph Edward Honore Garand, Dayton, Minn.; School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, 1899; aged 63; died, Dec. 12, 1937, of bronchopneumonia and diabetes mellitus.

Charles Edwin Jenkins, Brookfield, Mo.; Rush Medical College, Chicago, 1900; member of the Missouri State Medical Association; veteran of the Spanish-American and World wars; aged 67; died, January 29, of cerebral hemorrhage.

Martha Estelle Hixson, East Lansing, Mich.; Grand Rapids Medical College, 1907; formerly a member of the board of education of Grand Ledge; aged 70; died, January 1, in Haslett, of cerebral hemorrhage and hypertension.

Mary E. Hagadorn, Pasadena, Calif.; University of Southern California College of Medicine, Los Angeles, 1892; member of the Associated Anesthetists of the United States and Canada; aged 80; died, January 4, of chronic myocarditis.

Ralph Dart ✠ Rock Island, Ill.; Rush Medical College, Chicago, 1903; past president of the Rock Island County Medical Society; at one time health commissioner; aged 57; died suddenly, January 15, of coronary occlusion.

William Thomas Heffernan, Spring Valley, Calif.; Medical College of Ohio, Cincinnati, 1889; member of the California Medical Association; aged 78; died, Dec. 30, 1937, of cerebral hemorrhage and bronchopneumonia.

Beresford Harty Thompson ✠ Brooklyn; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1908; served during the World War; aged 52; died, in December 1937, in St. John's Hospital, of coronary thrombosis.

Benjamin B. Griffith, Vincennes, Ind.; Jefferson School of Medicine, Louisville, 1882; Missouri Medical College, St. Louis, 1884; member of the Indiana State Medical Association; aged 75; died, January 16, of coronary occlusion.

Shubel M. Moulton, Minneapolis; University of Louisville (Ky.) Medical Department, 1892; Northwestern University Medical School, Chicago, 1893; aged 71; died, January 22, in the Swedish Hospital, of lobar pneumonia.

Edwin R. Hickerson, Moberly, Mo.; St. Louis Medical College, 1885; member of the Missouri State Medical Association; on the staff of the Wabash Employee's Hospital; aged 76; died, January 4, of coronary thrombosis.

Louis Mackler ✠ Atlantic City, N. J.; Jefferson Medical College of Philadelphia, 1917; served during the World War; aged 42; was drowned, January 11, near Bel Air, Md., when his car skidded and went into a stream.

Simon Gurewitch, Chicago; St. Louis College of Physicians and Surgeons, 1917; Chicago Medical School, 1922; aged 56; died, January 24, in the Michael Reese Hospital, of generalized peritonitis, secondary to cholecystitis.

William Edgar Othello Johnson, Madison, Mo.; Louisville (Ky.) Medical College, 1884; for many years county coroner; aged 81; died, Dec. 3, 1937, in the McCormick Hospital, Moberly, of chronic nephritis.

Ira Wilson Ellis, Murphysboro, Ill.; Medical College of Indiana, Indianapolis, 1883; formerly mayor; aged 79; on the staff of St. Andrew's Hospital, where he died, January 20, of carcinoma of the ascending colon.

Jacob Frederick Stock, Woodbury, Pa.; Jefferson Medical College of Philadelphia, 1890; aged 83; died, Dec. 4, 1937, in the Nason Hospital, Roaring Spring, of bronchopneumonia, chronic nephritis and myocarditis.

Henry M. Allen, Leesville, La.; College of Physicians and Surgeons, Dallas, Texas, 1907; parish coroner; aged 59; died, January 21, in the Baptist Hospital, Alexandria, of encephalitis, influenza and bronchopneumonia.

Paul Sheldon Scholes, Canton, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; served during the World War; aged 67; died, Dec. 9, 1937, of paralysis agitans.

Reuben Hills Bemish, Darien, Conn.; University of Pennsylvania Department of Medicine, Philadelphia, 1887; aged 71; died, January 8, in the Stamford (Conn.) Hospital, of myocarditis and arteriosclerosis.

Harry B. Carty, Freemansburg, Pa.; Medico-Chirurgical College of Philadelphia, 1899; member of the Medical Society of the State of Pennsylvania; aged 60; died, Dec. 9, 1937, of nephritis and hypertension.

Archibald Armstrong Livingston, Cedar Hill, Mo.; St. Louis College of Physicians and Surgeons, 1907; aged 66; died, January 16, in the Rosiclare (Ill.) Hospital, of arteriosclerosis and cerebral hemorrhage.

James Maxwell Ware, Magnolia, Texas (licensed in Texas, under the Act of 1907); member of the State Medical Association of Texas; aged 60; died, Dec. 20, 1937, of carcinoma of the liver and intestine.

Charles H. Kaiser, Hillsboro, Kan.; Kansas Medical College, Medical Department of Washburn College, Topeka, 1900; member of the Kansas Medical Society; aged 64; died, January 2, of coronary occlusion.

John J. Bethea, Hattiesburg, Miss.; Tulane University of Louisiana Medical Department, New Orleans, 1889; aged 74; died, January 24, in the Methodist Hospital, of metastatic carcinoma of the lung.

Charles Obra Cron, Camp Douglas, Wis.; College of Physicians and Surgeons, Keokuk, Iowa, 1896; member of the State Medical Society of Wisconsin; aged 65; died, January 2, of coronary disease.

Alvah Graves Ray ⊕ Jackson, Ohio; Kentucky School of Medicine, Louisville, 1894; member and past president of the city board of education; aged 70; died, January 19, in an automobile accident.

Arthur Spencer Ayres, Indianapolis; University of Vermont College of Medicine, Burlington, 1888; member of the Indiana State Medical Association; aged 74; died, January 19, of pneumonia.

Thomas Edward Horner ⊕ Atchison, Kan.; Kentucky School of Medicine, Louisville, 1897; aged 62; on the staff of the Atchison Hospital, where he died, January 16, of coronary thrombosis.

Robert Beatty Castree, Ballston Spa, N. Y.; Albany (N. Y.) Medical College, 1901; for many years county coroner and jail physician; aged 61; died, Dec. 28, 1937, of coronary thrombosis.

Frederick J. Burgess, Hot Springs National Park, Ark.; College of Physicians and Surgeons, Little Rock, 1910; aged 54; died, January 27, of septicemia, acute nephritis and diabetes mellitus.

George W. Bromell, Denver; Eclectic Medical University, Kansas City, Mo., 1911; member of the city board of health; aged 69; died, January 23, in Atlanta, Ga., of chronic myocarditis.

Henry Bernhardt Weiper, Lower Lake, Calif.; Rush Medical College, Chicago, 1884; at one time mayor of Durand, Wis.; formerly health officer; aged 89; died, Dec. 11, 1937, of pneumonia.

Clifford Walcott Kellogg, Higganum, Conn.; Yale University School of Medicine, New Haven, 1896; aged 76; died, January 31, in the Middlesex Hospital, Middletown, of pneumonia.

Charles Barland Hogeboom, Huntsville, Ala.; Medical Department of Grant University, Chattanooga, Tenn., 1900; aged 60; died suddenly, January 12, of acute dilatation of the heart.

Elmer Hoffman, Sharon, Wis. (licensed in Wisconsin under the Act of 1899); aged 74; died, January 28, in the Walworth County Hospital, Elkhorn, of nephritis and chronic myocarditis.

George Fellows McCormack, New Orleans; Hahnemann Medical College and Hospital, Chicago, 1906; aged 54; was found dead, January 14, of hemorrhage and shock due to a fall.

Louis Edward Madden, Denver; University of Colorado School of Medicine, Denver, 1927; on the staff of St. Joseph's Hospital; aged 39; died, January 21, of pulmonary tuberculosis.

Frances Margaret Lane, Cody, Wyo.; Hering Medical College, Chicago, 1898; member of the Wyoming State Medical Society; aged 59; died, January 19, of influenza and pneumonia.

John Peters Rothermel, Reading, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1889; aged 71; died, Dec. 6, 1937, of coronary thrombosis and arteriosclerosis.

Raymond Hensel, Niagara Falls, N. Y.; Albany Medical College, 1913; member of the Medical Society of the State of New York; aged 47; died, Dec. 2, 1937, of coronary thrombosis.

Oscar Frederick Ziegler ⊕ Wildwood, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1921; aged 40; died, Dec. 19, 1937, of angina pectoris and valvular heart disease.

Agnes Emilie Hansen, Santa Ana, Calif.; College of Physicians and Surgeons of San Francisco, 1907; aged 55; died, Dec. 19, 1937, of shock and exhaustion due to a crushed chest.

Robert Judson Sharp, Columbus, Ohio; University of the City of New York Medical Department, 1883; aged 83; died, Dec. 15, 1937, of lobar pneumonia and chronic myocarditis.

Lynn H. Parker, Parsons, Kan.; Kansas City Hahnemann Medical College, 1914; member of the Kansas Medical Society; aged 51; was killed, January 2, in an automobile accident.

William H. Monahan, Jackson, Ohio; Medical College of Ohio, Cincinnati, 1874; for many years county coroner; aged 87; was found dead, January 18, of cerebral hemorrhage.

Edgar Henry Howell ⊕ San Francisco; Hahnemann Medical College of the Pacific, San Francisco, 1907; aged 54; died, Dec. 30, 1937, of coronary thrombosis and myocarditis.

Augustine T. Holcomb, Novi, Mich.; Western Reserve University Medical Department, Cleveland, 1884; aged 76; died, January 18, in a hospital at Northville, of pneumonia.

Walter C. Whiting, West Bridgewater, Mass.; Yale University School of Medicine, New Haven, 1881; aged 79; died, Dec. 8, 1937, of paralysis agitans and arteriosclerosis.

William H. Borget, Buffalo; Toledo Medical College, 1886; aged 80; died, January 12, in the Douglas Memorial Hospital, Fort Erie, Ont., Canada, of Adams-Stokes syndrome.

Henry Randolph Garland, Washington, D. C.; Columbian University Medical Department, Washington, 1897; aged 81; died, January 2, of arteriosclerosis and myocarditis.

Uriah C. Carson, Long Beach, Calif.; Cincinnati College of Medicine and Surgery, 1878; aged 82; died, Dec. 26, 1937, of carcinoma of the prostate, nephritis and uremia.

Walter Lenehan, Standish, Mich.; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; aged 60; died, January 17, in a sanatorium at Howell, of pneumonia.

Douglas Wallace, Winnipeg, Manit., Canada; Manitoba Medical College, Winnipeg, 1913; aged 53; died, Dec. 23, 1937, in the Winnipeg General Hospital, of endocarditis.

James T. Eslin, Washington, D. C.; Georgetown University School of Medicine, Washington, 1891; aged 80; died in January, of accidental illuminating gas poisoning.

John Bristol Yates, Denver; Kentucky University Medical Department, Louisville, 1905; aged 60; died, Dec. 23, 1937, of myocarditis, pulmonary tuberculosis and nephritis.

Thomas Arthur Graven ⊕ Wooster, Ohio; Jefferson Medical College of Philadelphia, 1900; served during the World War; aged 67; died, January 24, of myocarditis.

Thomas Richards Griffith, Riverside, Calif.; Boston University School of Medicine, 1898; aged 72; died, Dec. 18, 1937, of arteriosclerosis, renal insufficiency and uremia.

William A. Brantley, Atlanta, Ga.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1897; aged 88; died, January 3, of bronchopneumonia and influenza.

Robert Long Boling, San Francisco; University Medical College of Kansas City, Mo., 1897; aged 70; died, Dec. 21, 1937, of myocarditis and hypertrophy of the prostate.

Robert Rush Goad ✠ Hillsville, Va.; University College of Medicine, Richmond, 1911; bank president; aged 53; died suddenly, January 27, of coronary thrombosis.

Charles Adolph Erickson, Rockford, Ill.; Chicago College of Medicine and Surgery, 1910; aged 60; died, January 24, in St. Anthony's Hospital, of bronchopneumonia.

Rufus Henry Finefrock, Prospect, Ohio; Starling Medical College, Columbus, 1896; formerly state senator; aged 67; was killed, January 12, in an automobile accident.

George R. Logan, Enterprise, Ky.; Kentucky School of Medicine, Louisville, 1890; aged 81; died, January 20, in St. Joseph's Hospital, Lexington, of pneumonia.

Joseph Edward Gavin, New York; University and Bellevue Hospital Medical College, New York, 1917; aged 62; died, January 26, in Miami, Fla., of heart disease.

William Grant Bird, Fenton, Mich.; Detroit College of Medicine, 1895; fellow of the American College of Surgeons; aged 69; died, January 21, of heart disease.

Charles Nathan Caton, Wynona, Okla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1901; aged 61; died, Dec. 26, 1937, of coronary thrombosis.

Patrick E. Mills ✠ Chicago; Northwestern University Medical School, Chicago, 1901; aged 65; died, January 9, in the Mercy Hospital, of carcinoma of the liver.

F. Emerson Daigneau, Austin, Minn.; University of Vermont College of Medicine, Burlington, 1886; aged 75; died, Dec. 10, 1937, of coronary disease and nephritis.

Edward P. Greene, Campbell, Calif.; State University of Iowa College of Homeopathic Medicine, Iowa City, 1888; aged 78; died, Dec. 24, 1937, of myocarditis.

John D. Leith, McCreary, Manit., Canada; Trinity Medical College, Toronto, Ont., 1894; aged 76; died, Dec. 14, 1937, of bronchopneumonia and arteriosclerosis.

Charles W. Day, New York; Hahnemann Medical College and Hospital, Chicago, 1892; Civil War veteran; aged 89; died, January 19, of angina pectoris.

Alexander B. Davis, Wilson, Okla.; University of Tennessee Medical Department, Nashville, 1893; aged 80; died, January 12, of cerebral hemorrhage.

William T. Beebe, Washington, N. C.; Howard University College of Medicine, Washington, D. C.; 1906; aged 58; died, Dec. 11, 1937, of bronchopneumonia.

Alfred Peter Holz ✠ Seymour, Wis.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1898; aged 64; died, January 22, of chronic myocarditis.

Chauncey David Creviston, Houston, Texas; Starling Medical College, Columbus, 1900; aged 64; died, Dec. 22, 1937, of bronchopneumonia and influenza.

Arthur Bryant Moss, Lincoln, Neb.; Jenner Medical College, Chicago, 1908; aged 54; died, January 28, of mesenteric thrombosis and hepatic carcinoma.

Lewis C. Cowen, Rising Sun, Ind.; Medical College of Ohio, Cincinnati, 1874; aged 89; died, January 27, of arteriosclerosis and cerebral hemorrhage.

Jackson B. Shepard, Philadelphia; Howard University College of Medicine, Washington, D. C., 1894; aged 68; died, Dec. 27, 1937, of hypertensive nephritis.

Naaman Cyrus Miller, Fostoria, Ohio; Western Reserve University Medical Department, Cleveland, 1882; aged 79; died, January 28, of chronic arthritis.

Frank Orson Mosher, San Bernardino, Calif.; Dartmouth Medical School, Hanover, N. H., 1896; aged 70; died, Dec. 12, 1937, of pulmonary tuberculosis.

Francis Fenelon Johnson, San Francisco; Cooper Medical College, San Francisco, 1894; aged 68; died, Dec. 21, 1937, of arteriosclerosis and myocarditis.

Lee D. Robinson, Halleck, Mo.; Northwestern Medical College, St. Joseph, 1892; aged 78; died, Dec. 23, 1937, in St. Joseph, of chronic myocarditis.

Septimus Jasper Kell, Bluefield, W. Va.; College of Physicians and Surgeons, Baltimore, 1907; aged 57; died suddenly, January 12, of angina pectoris.

Charles Allison Foulks, Kansas City, Kan.; Chicago Medical College, 1885; aged 79; died, Dec. 23, 1937, in Compton, Calif., of coronary thrombosis.

Charles F. Bassett, Chicago; Chicago Homeopathic Medical College, 1879; aged 87; died, Dec. 19, 1937, in Altadena, Calif., of coronary thrombosis.

Lorenzo Dow Latham, Tulsa, Okla.; St. Louis College of Physicians and Surgeons, 1896; aged 74; died, Dec. 11, 1937, in Vinita, of lobar pneumonia.

Ross Whittaker Loomis, Toledo, Ohio; Toledo Medical College, 1903; aged 57; died, Dec. 22, 1937, of aortic insufficiency and bronchopneumonia.

John L. Livingstone, Long Beach, Calif.; Michigan College of Medicine, Detroit, 1883; aged 83; died, Dec. 29, 1937, of carcinoma of the stomach.

Guernsey Reiner Lunger, Seattle; University of Cincinnati College of Medicine, 1922; aged 40; died, Dec. 26, 1937, of pulmonary tuberculosis.

Alfred J. Harris, McAlester, Okla.; Missouri Medical College, St. Louis, 1877; Confederate veteran; aged 96; died, January 21, of pneumonia.

Thomas Rea ✠ Yreka, Calif.; Oakland College of Medicine and Surgery, 1913; aged 57; died, Dec. 1, 1937, of coronary heart disease and aortitis.

Ezra Adonis Shippey, Broaddus, Texas (licensed in Texas under the Act of 1907); aged 69; was found dead in bed, Dec. 28, 1937, of endocarditis.

William S. Brownell, Detroit; Detroit College of Medicine, 1892; served during the World War; aged 69; died, January 24, of coronary thrombosis.

Sidney Avery Clark ✠ Northampton, Mass.; Harvard University Medical School, Boston, 1891; aged 72; died, January 14, of coronary thrombosis.

Hamilton Worth Emanuel, Milnor, N. D.; Fort Wayne (Ind.) College of Medicine, 1880; aged 80; died, January 4, of coronary occlusion.

Welch Michael Powers, Tacoma, Wash.; Creighton University School of Medicine, Omaha, 1934; aged 29; died, January 8, of pneumonia.

Edward Hood Julien, Yreka, Calif.; Detroit College of Medicine, 1895; aged 66; died, Dec. 16, 1937, of uremia and gastric hemorrhage.

Charles Ross Campbell, Chester, W. Va.; Starling Medical College, Columbus, 1903; aged 60; died, January 11, of chronic myocarditis.

Angus Bethune Patterson, Barnwell, S. C.; Louisville (Ky.) Medical College, 1871; aged 86; died, January 27, of bronchopneumonia.

Henry Blakeslee Boyden, Grand Island, Neb.; Rush Medical College, Chicago, 1911; aged 48; died, Dec. 9, 1937, of lobar pneumonia.

William James Gavin, Greensburg, Ind.; Miami Medical College, Cincinnati, 1880; aged 82; died suddenly, January 19, of heart disease.

Enos Bohnett, Sterling, Ill.; Bennett Medical College, Chicago, 1899; aged 71; died, Dec. 13, 1937, in East Moline, of myocarditis.

William H. Cohee, Marietta, Ind.; Medical College of Indiana, Indianapolis, 1898; aged 70; died, January 19, of coronary occlusion.

Harold Spenceley, Shedden, Ont., Canada; Queen's University Faculty of Medicine, Kingston, 1924; aged 42; died, Dec. 4, 1937.

H. L. Jordan, Pine Bluff, Ark.; Meharry Medical College, Nashville, Tenn., 1903; aged 65; died, January 14, of cerebral hemorrhage.

Charles Ray Parker, Chicago; Chicago College of Medicine and Surgery, 1913; aged 57; died, January 10, in St. Petersburg, Fla.

Nelson A. Sloan, Brighton, Iowa; Syracuse (N. Y.) University College of Medicine, 1888; aged 74; died, Dec. 7, 1937, of uremia.

John Cecil White ✠ Blackstone, Va.; Medical College of Virginia, Richmond, 1927; aged 37; died, Dec. 31, 1937, of heart disease.

Florence Howard Bullis, St. Louis; American Medical College, St. Louis, 1912; aged 60; died, January 6, of heart disease.

Frank Sydney Rounthwaite, Toronto, Ont., Canada; Trinity Medical College, Toronto, 1895; aged 65; died, Dec. 15, 1937.

Albert C. Broell, Chicago; Chicago Medical College, 1886; aged 73; died, January 9, of carcinoma of the right tonsil.

William Stanley Mhoon, Philipp, Miss. (licensed in Mississippi in 1911); aged 54; died, January 5, of pneumonia.

Zachariah T. Goolsby, Mexia, Texas; Barnes Medical College, St. Louis, 1897; aged 68; died, Dec. 24, 1937.

Correspondence

ABSORPTION OF DRUGS AND POISONS THROUGH THE SKIN

To the Editor:—These comments are prompted by the report of David I. Macht's experiments (The Absorption of Drugs and Poisons Through the Skin and Mucous Membranes, THE JOURNAL, February 5, p. 409). Macht incorporated drugs in fixed fats, observed systemic reactions of the drugs, and concluded: "Such experiments revealed that none of the fixed fats carrying potent drugs were absorbed very readily." If writers on this subject would use the word "absorption" only when they refer to absorption of substances into the blood stream, and "penetration" only when they refer to penetration of substances into or through the skin, much confusion and also, sometimes, faulty deductions would be avoided. Macht, of course, is speaking of penetration into the skin, for certainly he would not expect a fixed fat to be absorbed into the circulation through the skin.

Macht believes that his results should have "great practical significance, particularly to dermatologists," but in dermatologic practice the question of penetration is far more important than that of absorption and on this his experiments throw no light, by reason of the fact that penetration cannot be measured in terms of systemic reaction:

EXPERIMENT 1.—Into a test tube run a few cubic centimeters of melted lard containing 2 per cent of salicylic acid. Allow it to harden and overlay with a few cubic centimeters of a 20 per cent solution of ferric chloride. Color reaction diffuses quickly throughout supernatant fluid, demonstrating diffusion of salicylic acid into the aqueous ferric chloride solution.

EXPERIMENT 2.—Same as experiment 1, but substitute petrolatum for lard. No appreciable diffusion of salicylic acid into the ferric chloride follows.

Assume that when the salicylic acid-lard combination is rubbed on the skin it penetrates to the subcutaneous layer: there follows free release and diffusion of salicylic acid into the constantly flowing aqueous circulation.

Assume that when the salicylic acid-petrolatum combination is rubbed on the skin it penetrates as well as the lard combination: there follows no release and no diffusion into the circulation.

This indicates that two different vehicles may penetrate the skin equally well but show widely different systemic reactions.

Unlike fixed oils, essential oils may conceivably be absorbed directly into the circulation but only to the extent to which they are soluble in water.

EXPERIMENT 3.—In a small test tube place 1 cc. of methyl salicylate and overlay with 1 cc. of 20 per cent ferric chloride. A characteristic blue ring forms immediately and color diffuses upward, being quickly discernible throughout the overlying fluid.

This experiment records the diffusion of dissolved methyl salicylate from the oil-water interface. In the experiment this interface is relatively small compared with the total volume of oil. If, however, the 1 cc. of oil is spread over a large area of skin the relative interface area is tremendously increased and further, if one considers that now the water side of the interface is a constantly flowing stream, one perceives a possible clue to Macht's experimental observations.

If this is the answer, should it not lead to the conclusion that water itself is the most suitable vehicle? It probably would be were it not for the outer lipocorneal layer, through which water does not pass. It is conceivable that essential oils pierce this barrier more readily than fixed oils, but there is nothing in Macht's experiments to prove or disprove it.

The problem of skin penetration and absorption of substances into the circulation is far more than a mechanical one; it involves many physicochemical and biologic considerations as varied as the substances with which one deals. Not until these problems have been solved will the local treatment of skin disorders be placed on a really rational basis.

Take, for example, the official boric acid ointment, with which I have experimented:

EXPERIMENT 4.—Saturate a strip of blue litmus paper with water, place on a glass slide and cover with boric acid ointment, U. S. P. Observe the reverse side for the action of boric acid on the blue litmus paper, which should turn pink. After several hours the paper is still blue, showing that there has been virtually no penetration of boric acid into the moist litmus paper.

It can rationally be deduced that when this ointment is used on wounds or ulcers and on those skin disorders in which the lesions are bathed in aqueous secretions, it can have little or no effect, at least as far as the boric acid is concerned. However, the petrolatum can be treated to permit ready release of the boric acid.

While petrolatum virtually locks up boric acid, it releases other substances quite readily. It is obvious that intelligent control of this release factor for various vehicles and drugs would be a distinct advance in the local treatment of skin disorders.

My experiments have convinced me that there will probably never be such a thing as a universal ointment vehicle which is better than any other vehicle. On the contrary, I believe that the more the problem is studied the more it will be realized that vehicles should be individualized in accordance with the drugs used, the therapeutic aim, and special needs of the disorder to be treated.

J. J. SEELMAN, M.D., Milwaukee.

HIGH HUMAN TEMPERATURE

To the Editor:—In Queries and Minor Notes in THE JOURNAL, February 5, page 461, in a discussion of the highest temperature that the human body can reach and still survive, doubt is expressed as to temperatures higher than 108 F. While testing the efficacy of different anti-scarlet fever serums administered intravenously to patients with scarlet fever at the Willard Parker Hospital during the years 1930-1932, I observed survival repeatedly following temperatures of 107 or 108, and occasionally after higher ones—in one case even after a temperature of 110 F. Unquestionably more temperatures greater than 108 F. would have been seen if immediate means for their reduction had not been instituted. However, when a temperature of 107 F. was reached, about a degree lower in children, the patient began to get restless and delirious so that drastic antipyretic measures had to be commenced. These consisted of continuous colonic flushing with ice, as milder measures were found to be useless. For example, in one case, alcohol sponges, acetylsalicylic acid, an ice cap and fluids did not reduce the temperature but on the contrary it kept on rising till it reached 109 F., when the patient died. The patient who had a temperature of 110 F. was given continuous colonic flushing with ice for twenty minutes but the temperature was still 108 in the axilla, 107 after a half an hour, and 102 F. at the end of forty-five minutes, when the treatment was discontinued. In the morning, which happened to be six hours later, the temperature was normal and remained normal until the day of discharge, with the patient showing no ill effects from having been at the point of death. These were elevated temperatures for short periods which usually came about an hour following the administration of the antitoxin and in the majority of instances were preceded by a chill, although the patient with the temperature of 110 F. did not have a chill. In order to prevent any tragic end, the onset of these temperatures had to be watched for carefully. How-

ever, if they were promptly treated no harmful results were observed. These were all rectal temperatures. Thus, the human body can survive a temperature of 110 F. and possibly even higher for a short duration and not suffer any discernible adverse consequences.

FERDINAND G. KOJIS, M.D., New York.

TESTOSTERONE PROPRIONATE

To the Editor:—In view of the unwarranted and apparently nation-wide publicity that our paper which was read before the local medical society the other evening received, we think it expedient to publish this statement.

We gave a preliminary report concerning our studies with testosterone proprionate before the Baltimore Medical Society on the evening of March 4, and an entirely erroneous newspaper report has spread throughout the country. Our paper reported only a part of our work on patients with hypogonadism, either primary or due to castration. In these the results were very promising. We made no reference to rejuvenating senile men or men with psychic impotence and that sort of condition. However, it seems that an entirely wrong interpretation has been taken by the press reports, and we feel that physicians who have not used this drug should be made aware that we have used enormous dosages, which are not yet practical for routine purposes in other fields, that our work is entirely experimental and preliminary and that there is no occasion for any widespread use as yet among the members of the medical profession. It is most unfortunate and regrettable that the public and the members of the medical profession should have their attention called to an apparently valuable drug in such a manner.

As you are probably aware, the development of testosterone is not original on our part, and there are other clinics, both here and abroad, that are making the same clinical observations. We regret exceedingly that our report before the local medical society was misinterpreted.

JOHN EAGER HOWARD, M.D.
SAMUEL A. VEST, M.D.
Baltimore.

SELENIUM POISONING

To the Editor:—In your issue of Dec. 25, 1937, under Current Comment you report on the retention and elimination of selenium in an article by M. I. Smith, B. B. Westfall and E. F. Stohlman Jr. (*Pub. Health. Rep.* **52**:1171 [Aug. 27] 1937). By implication one may infer that interruption of ingestion of selenium is followed by its removal from the system and cessation of injury.

The paper by Dr. Hazel E. Munsell, Grace M. DeVaney and Mary H. Kennedy indicates that such injury persists even though the selenium is removed from the animal body. Also it shows rather conclusively that organic selenium is of the same order of toxicity as sodium selenite. This is also shown by the work of the late Dr. Kurt Franke of South Dakota and his associates. A summary of the data along this line is given in Bulletin 311, Alkali Disease or Selenium Poisoning, by Alvin L. Moxon of the South Dakota Agricultural Experiment Station, Brookings, S. D. (1937). Unfortunately I have no extra copy of this paper to send you.

We have abundant information through our work to indicate the probability that organic selenium in green plants is fully as toxic or at least as quickly available as inorganic selenium.

HORACE G. BYERS, Washington, D. C.
Chief, Soil Chemistry and Physics Research Division, Bureau of Chemistry and Soils, U. S. Department of Agriculture.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

HEALTHY CHILD OF SYPHILITIC PARENT

To the Editor:—A woman, aged 46, married, has syphilis, contracted at 23 years of age and untreated until the present time. A son, aged 19, has a positive Wassermann reaction, Hutchinson's teeth and syphilitic iriditis. He is under treatment at present. A daughter, aged 10, has negative Wassermann and Kahn reactions on repeated tests and after a provocative injection of arsphenamine. I have discussed the negative reaction of this girl with several competent syphilologists and they are divided as to the necessity of antisyphilitic treatment. Is it possible that this young girl is entirely free? Kindly advise me what course to adopt in this case.

M.D., Quebec.

ANSWER.—The evidence offered with regard to the 10 year old daughter indicates that the child does not have congenital syphilis. The absence of signs of congenital syphilis and the repeatedly negative reactions are sufficient evidence to eliminate the possibility of syphilis even though the mother has syphilis and a brother has the congenital form of the disease. It is not uncommon for the oldest child of a family to have congenital syphilis while the younger children manifest neither clinical nor serologic signs of it. In view of the absence of confirmatory signs in the 10 year old daughter in question there is no need to treat her for syphilis as she probably does not have the disease.

LAUGHLEN TEST FOR SYPHILIS

To the Editor:—Is the Laughlen test for syphilis as reliable and dependable as the Wassermann, the Kahn, the Kline, the Meinecke, Kolmer's or any other modern and trustworthy test for syphilis? Is it an office procedure? About how long would it take to execute that particular test for syphilis? What special equipment will be required to perform this test in the office? How much would it cost, and where can such equipment be procured? Where can the antigen be obtained for the performance of the Laughlen test; what is its price? How long will it keep without spoiling? What is the technic of the Laughlen test for syphilis? In the case of inaccessible veins occasionally encountered in obese individuals, in infants and others, can blood be drawn for that test from either a finger or the lobe of an ear, or must it necessarily be drawn from a vein?

EMILIO L. HERGERT, M.D., Brooklyn.

ANSWER.—The questions raised in this letter are of considerable importance, particularly in connection with present-day interest in campaigns against syphilis. Instead of answering these questions directly, it may be well to ask When may a test for syphilis be considered trustworthy? Until recently it was assumed that for a new test to gain a foothold it must be subjected to trials in many different laboratories and, as indicated by numerous publications, most of these trials must lead to satisfactory results. The Kahn test, for example, was described in its present form in 1923, yet not until 1928, when the test was demonstrated at the League of Nations Conference at Copenhagen, did the test begin to gain recognition and, during that year, Kahn listed nearly 250 references to this test. Now, however, the publication of a new method or modification attracts almost immediate interest. This fact, however, does not mean that a new and relatively untried method may safely be used as a diagnostic agent for syphilis. Indeed, during the past several years an author of a new method or modification has been having an excellent opportunity to prove the worth of his particular test by including it in the Evaluation Studies of Tests for Syphilis carried on yearly by the United States Public Health Service. These studies throw light not only on the specificity and sensitivity of a given test but also whether or not this test compares favorably with the more established American tests.

The Laughlen test was described in the *Canadian Medical Association Journal* (**33**:179 [Aug.] 1935) and Robinson and Stroud spoke of it favorably in a note in THE JOURNAL (April 3, 1937, p. 1170), claiming 93 per cent agreement with the Wassermann test and 97 per cent agreement with the Kahn test. The test utilizes Kahn antigen to which has been added balsam and a dye. A drop of the antigen reagent is mixed with a drop of serum on a slide and the results are read by means of the microscope. The Laughlen antigen with full directions for its use may be obtained from the Lederle Laboratories of New York, which has been advertising the test as an office procedure. Actually, with the present-day availability of private, hospital

and public health laboratories, there seems to be no excuse for physicians to perform tests for syphilis in their office in connection with their practice. A laboratory method is of clinical value provided the method is of established reliability and is performed by one who is expert in the particular method. Many might add a third condition; namely, that the one who performs it should not be familiar with the clinical diagnosis, if any. If a physician has a strong feeling that the clinical diagnosis in a given patient is syphilis, he may not be psychologically fit to read the result of a test on the blood serum of the patient.

Blood may be obtained from a finger or ear lobe for practically all available tests for syphilis.

PURULENT DISCHARGE FROM NIPPLE AND CANCER

To the Editor:—Several patients with large breasts and inverted nipples discharging purulent material have recently consulted me. Is this a contributing cause of cancer of the breast? What can be done for these patients?

M.D., California.

ANSWER.—It is important to decide whether the purulent material actually comes from the nipple or whether it is simply an accumulation on the depressed nipple. Not infrequently when a nipple is below the surface of the breast, especially in women with large, fat breasts, foreign material such as perspiration or dirt may accumulate in the depressed area and result in a purulent discharge. This is especially true if women do not take particular pains to cleanse these inverted nipples properly. Hence the nipples should be elevated and gently squeezed to see whether the purulent material actually escapes from the ducts. If the purulent matter is due only to lack of sufficient cleanliness, the treatment is simple and the prognosis good. If, however, the purulent material comes from the ducts in the nipple it is essential to rule out the presence of cancer. A purulent discharge in the breast rarely causes cancer. On the other hand, it may often be caused by cancer. An examination of the breasts with the Cutter lamp or by an ordinary roentgenogram may be of assistance. The treatment of these purulent discharges should first be conservative. That is, hot moist dressings should be applied from time to time and also dry heat. If the discharge does not subside under this conservative management it is advisable to incise the involved area. If an abscess is encountered, incision is the proper treatment anyway. If a carcinoma is found, a radical operation must be performed immediately. Hence at the time of the exploratory incision, the operating room must be ready for a biopsy and radical operation.

AGRANULOCYTOSIS FROM AMINOPYRINE

To the Editor:—In the April issue of *Consumers Union* there is an article on Aminopyrine. Will you kindly inform me whether the use of this drug is as dangerous as this article indicates.

W. ALLEN GRIFFITH, M.D., Berwyn, Md.

ANSWER.—The query can be answered by stating that in the light of present knowledge the information in the article mentioned is essentially correct.

Certain points relative to the rôle of aminopyrine and other drugs in the production of agranulocytosis bear repeated emphasis. First, it is now generally accepted over the world that aminopyrine and its many combinations, including both proprietary and patented remedies for the relief of pain, are capable of producing agranulocytosis in an occasional person, presumably one that is sensitive or "allergic" to the drug. The nature of the sensitivity is not known. Furthermore, it is believed that a large amount of the drug is not necessary to produce depletion of the neutrophilic white cells. Apparently in an occasional patient this may result from only one or two doses of as little as 5 grains (0.03 Gm.) each. However, it seems that most cases develop after the long continued use of the drug.

Aminopyrine is an excellent pain relieving agent and for this reason it has been used as the essential ingredient in many patented remedies that are sold to the public without any indication as to its presence. Because of this, the disease still is seen mainly in persons who resort to self medication and purchase such remedies from drug stores. A list of some of these preparations was given by Kracke and Parker in THE JOURNAL, Sept. 21, 1935, page 960.

Physicians now use aminopyrine with caution, usually accompanied by careful checking of the blood picture. Because of this the disease has apparently decreased markedly from the high peak of more than 1,500 deaths in the United States alone in the three years that ended in 1934. It would appear that it is not safe to use aminopyrine and its combinations under any conditions, since there is the ever present chance that the patient may be sensitive to the drug; and, since the disease often develops abruptly and the white cells are depleted before it is recognized clinically, the use of the drug is always fraught with danger. It should be pointed out that there is evidence incriminating other drugs as etiologic agents in this disease. Most noteworthy of these is dinitrophenol, widely used as a fat reducing agent. Also in rare instances the disease can follow the use of arsphenamine and other organic arsenical compounds. Safe rules for physicians to follow are to refrain from the use of aminopyrine and dinitrophenol, so far as possible; if it is necessary to use them, the white cell count should be carefully checked at frequent intervals; patients should be cautioned against the purchase of these drugs and any other pain-relieving remedy on which the formula is not stated; constant activity should be exercised to promote legislation that will prohibit the unrestricted sale of such agents to the public. It seems likely that as long as these drugs are available for public consumption there will be agranulocytosis with its high mortality, but that, if they could be dispensed only on prescription, the disease might eventually disappear.

INSULIN IN DIABETES

To the Editor:—Moderately severe diabetes is sometimes treated with two doses of insulin (25 units each) given with the morning and evening meals, and little or no insulin with the noon meal. A says that "little or no insulin is required for the noon meal because the morning dose of insulin continues to act for six to eight hours, and so carries over its effect for the noon meal (which should be lower in carbohydrates)." B says that "the noon meal requires little or no insulin because of the increase in tolerance following the intake of carbohydrates in the morning (the noon meal should be rich in carbohydrates)." Please give the correct answer, with reasons; also references for further details.

ERWIN R. KABACK, M. D., New York.

ANSWER.—Both answers are partially correct. That the diabetic patient is at his worst in the morning, better at noon and best of all in the evening is almost a proverb. In the morning his storage of carbohydrate is low and, as all agree, whether in diabetes or in health that is the time he utilizes carbohydrate least well; at noon and by the night meal increasing quantities of carbohydrate have been brought into action and are being metabolized and in consequence the entire machine is running more normally. Many a diabetic patient can take 10 or 20 Gm. of carbohydrate on retiring and wake up sugar free.

The blood sugar, save in the mild cases, which would be ruled out by the premises of the question, is higher in the morning. One would burden it therefore with the least quantity of carbohydrate at a meal and in fact usually this is done by giving one fifth at breakfast and two fifths at each of the other two meals.

Exercise is eliminated at night, so the body begins the day without the advantage of it, but with the progress of the day its favoring influence becomes felt.

But why use regular insulin 25-0-25? Is not the blood sugar of the patient high on rising? Is not a retiring dose of 2, 3 or 4 units required on continued use of regular insulin? With protamine zinc insulin, possibly supplemented by regular insulin, presumably the blood sugar on rising would be nearer normal.

MECHOLYL IONTOPHORESIS IN VASCULAR DISEASE

To the Editor:—How efficacious is mecholyl in the treatment of chronic peripheral vascular disease, applied by iontophoresis?

M.D., Massachusetts.

ANSWER.—The administration of mecholyl (acetyl-beta-methylcholine chloride) by means of iontophoresis has been carefully studied for its value in the treatment of all common types of chronic peripheral vascular disease. It has not been found to be efficacious for patients with arteriosclerosis or arteriolosclerosis senilis, or arteriosclerosis with diabetes. It has not been of value in most cases in association with thromboangiitis obliterans. It has no effect on patients with chronic lymphedema. It is of established value for the healing of chronic varicose and postphlebitic ulcers and has healed many of these following the failure of varicose vein injections and other forms of treatment to heal them. It has a palliative effect in many cases of Raynaud's syndrome, reducing the number and intensity of the attacks but not affecting the course of the disease. In a considerable percentage of cases of scleroderma the course of the disease has been affected favorably, with loosening of the skin and a general increase in local circulation. Accompanying infection and nervous shocks or anxiety apparently prevent improvement in these cases and in some patients there has been unexplained lack of improvement. Patients suffering from mild spasms of the peripheral arterial tree due to trauma, such as the group known as "pneumatic

hammer disease," have been relieved of their symptoms in practically all instances by mecholyl iontophoresis.

It should be remembered that in general these conditions are chronic and that improvement from whatever method is inevitably slow. In most instances from thirty to fifty treatments are necessary before judgment as to the value of the method in an individual case can be rendered.

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SENSITIZATION TO EPINEPHRINE

To the Editor:—Several years ago, while having a dental extraction, I discovered that I was sensitive to epinephrine. About one year ago I had a foreign body removed from my left eye (cornea) and this was followed by a phlyctenular keratitis. I suffered excruciating pain as these spots appeared on the cornea. This continued until one day my physician said "This looks like an allergic eye." I then promptly informed him that there was only one thing I was sensitive to, and that was epinephrine. He stopped putting epinephrine into my eye and I stopped using phenacaine ointment (which contains epinephrine) and I made a rapid recovery. Since then I have been given an intradermal injection of epinephrine (wheal formation) and within two minutes I had palpitation, trembling, pallor, weakness, a rise in blood pressure of almost 40 mm. of mercury and a corresponding rise in pulse. Can a person be desensitized to epinephrine? What is the etiology of sensitization? What is the best procedure to follow?

M.D., New York.

ANSWER.—The sensitivity in question may be due to epinephrine, but in view of the fact that many epinephrine preparations contain preservatives this factor should also be considered as a possible causative agent. Not only the different brands vary as to the preservative used but different forms of the same brand frequently contain different preservatives. A great many people are oversensitive to epinephrine and have a lowered threshold to stimulation of the sympathetic system. No method of desensitization to the epinephrine itself is worth undertaking. Frequently such sensitivities are lessened by avoiding fatigue and maintaining good health.

MASTURBATION IN SMALL CHILD

To the Editor:—What is the treatment for a 2 year old boy who masturbates? The child has been circumcised. There are no discoverable physical defects.

M.D., New York.

ANSWER.—The treatment of masturbating children must begin with the correction of all local disorders in the region of the genitalia. The clothes should be of proper size so that the rubbing of tight clothes does not irritate the penis. Itching skin disorders, such as intertrigo or pediculosis, in the perianal region should be remedied; oxyuriasis (pinworms) if present should be eradicated and so on. Excessive fondling and excitation on the part of parents, servants or older children should be discouraged. Proper emotional balance, physical hygiene and healthful sleeping arrangements should be instituted in the home. Masturbation in a child may be just one manifestation of faulty emotional adjustments resulting from various factors, such as the parents prolonging his infancy by excessive "babying," excessive nagging and punishing, excessive attention and spoiling, or too much emotional excitment in playing with other children. Especially if this is an emotional child, a calm, properly balanced environment is essential. Mechanical restraint is definitely contraindicated. Avoid sending the youngster to bed as a punishment for some misdeed, because having nothing else to do and needing gratification gives impetus to the act. The child should be put to bed at night and for the afternoon nap only when he is tired enough to fall asleep at once, and not allowed to remain in bed in the morning unoccupied for a long time, as these are the times when the act is most practiced. During the day his time must be completely occupied by regulating his activities and never leaving him entirely to himself. The habit should not be made the topic of discussion in the presence of the child, nor should punitive measures, such as whipping, shaming, nagging, pleading or bribing, ever be used. Nor should he be told that it is dirty or naughty or that the habit will make him sick. A youngster should never be surprised or caught masturbating. When he is found indulging, without referring to the act, he should be given some pleasant and interesting task, or invited to play a game which will distract his attention from the genitalia and interrupt his preoccupations, in a manner which he has no occasion to resent. Close observation of these children is necessary, but not spying to the extent of arousing fear of being constantly suspected.

It is important to enlighten the family that no great harm will result and that in all probability even if it is ignored and nothing is done, a child of 2 years will sooner or later forget the habit and turn to other forms of amusement, especially if he is otherwise healthy, active and happy.

SWELLING AROUND EYES AFTER SEA BATHING

To the Editor:—During the month of August I treated two children, both suffering from a marked swelling about the eyes. The upper and lower lids were involved with soft swelling and apparently no inflammation. Both gave a history of having been bathing in the ocean the day before. The condition in each case was treated as one of angioneurotic edema, with repeated small injections of epinephrine and cold compresses locally. Both subsided within twelve hours without recurrence. Pain was absent throughout. Am I correct in assuming that these cases were on an allergic basis, possibly as reactions to cold sea water?

ATTILIO A. TRIPPITELLI, M.D., Brooklyn.

ANSWER.—It is not possible from the description to be sure that the diagnosis of angioneurotic edema is correct, although it seems quite probable. Angioneurotic edema is asymmetrical and rarely involves the two eyes at the same time. As to the cause of the swelling, hypersensitivity to cold may well be a factor. Many such cases have been reported and some serious results have occurred in certain patients who are sensitive to cold water. Some even believe that a certain percentage of drownings is due to anaphylactic shock that occurs in patients who are peculiarly hypersensitive to cold. It might be well to try cold applications to the eyes to see if any swelling will result. There is a possibility too that the swelling may be due merely to the irritation to the eyes (not allergic) from the salt contained in water.

COLLECTION AND PRESERVATION OF BLOOD FOR MAILING

To the Editor:—Please tell me how to take care of or preserve blood specimens for a Wassermann test. I am obliged to send my work to the state laboratory, and I keep the specimen on ice or in a freezer, see that serum is well separated and clear, and then mail it out. During the hot weather, many of my reports from the laboratory show that blood has hemolyzed. What can I do about it?

ERNEST BALL, M.D., Sulphur, Okla.

ANSWER.—The collection and preparation of the specimen of blood for shipment to the laboratory are perhaps the most important of the precautions to be taken in securing satisfactory results from serologic tests. Hemolysis is frequently due to the use of unsatisfactory outfits for bleeding. It may result from the retention of solutions if the syringes are sterilized by boiling or even from the force necessary to eject the blood from the syringe into the container. Syringes should not be used unless sterilized by dry heat. The sterilized outfits with Petroff needles are, in general, the most satisfactory and convenient.

In summer, hemolyzed specimens of blood received by mail are often found to be contaminated. A few bacteria that gain access at the time the specimen is collected and that would not render it unsatisfactory for serologic tests if kept for a day or two in the refrigerator or if the work could be undertaken promptly may multiply sufficiently in transit during warm weather to hemolyze the blood. Thus, aseptic precautions should be observed in the collection of blood specimens to avoid contamination, particularly when the specimen is to be subjected to temperatures that favor bacterial growth.

APPARATUS FOR MECHOLYL IONTOPHORESIS

To the Editor:—I am interested in the administration of mecholyl by iontophoresis. Can you suggest where I might obtain the necessary apparatus? Can you also list the necessary parts in making a simple galvanic machine?

M.D., Michigan.

ANSWER.—A simple galvanic machine for administering mecholyl by iontophoresis can be assembled from standard parts obtained from, or through, any radio repair store. The following is a list of the parts: one steel cabinet (Bud No. 993), one 50 ma. milliameter (Triplett No. 321), one 10,000 ohm variable resistance (Yaxley E-10M-P) with knob, one fuseholder and three 1/16 ampere fuses, one B battery (Burgess No. 5308 for use in cabinet or No. 10308 for longer life, or both), one single insulated tip jack, one twin insulated tip jack, 30 feet of braided wire (Kinkless RC), three tip plugs for attaching one end of lead wires to tip jacks, three insulated alligator clips for attaching the other end of the wires to electrodes (2 positive, one negative electrode) and two insulated spade lugs for attaching two short wires (2 feet long) to the battery.

Salesman 3 of the Radio Department of M. and H. Sporting Goods Store, 512 Market Street, Philadelphia, will assemble these parts and supply a convenient wooden brace for holding the battery in place. Makers of other machines for this purpose are the Valverde Laboratories, 252 Lafayette Street, New York, and William Balardo, 3102 Kingsbridge Avenue, Bronx, New York.

PARENTERAL ADMINISTRATION OF IRON

To the Editor:—What is the least painful preparation of iron (with strychnine) that can be used for parenteral administration? I have been using Fraisse's Ferrugineous Compound Ampoules (Fougera & Co.) but my patients complain of severe pain following injection.

EDWARD GIPSTEIN, M.D., New London, Conn.

ANSWER.—The "green iron and ammonium citrates" (now official) is considered the preferable iron preparation for injection purposes, it being claimed that its higher ammonium citrate content as compared with the "iron and ammonium citrates" (of garnet red color) renders it less protein precipitant and therefore its injection less painful. The facts that manufacturers (e. g., Parke, Davis & Co.) prefer to market it in ampules (of 0.015, 0.05 and 0.10 Gm.) also containing 0.005 Gm. of the local anesthetic quinine and urea hydrochloride, and that it should be given by intramuscular rather than subcutaneous injection, suggest that the problem of painless iron preparation for injection purposes has not yet been solved to entire satisfaction. There is no reason why the desired dose of strychnine nitrate may not be added to the iron solution just before injection. There is, however, no good reason for injecting the strychnine at all, because when the "tonic" effect of strychnine is desired it had better be given in divided doses throughout the day rather than reliance being placed on the effect of an injected single dose that is eliminated from the system within a few hours.

TRANSFER OF UNDULANT FEVER

To the Editor:—Are there any records of transfer of undulant fever from one human being to another, such as by blood transfusion or by a child nursing?

M.D., Tennessee.

ANSWER.—Although the possibility of transmitting brucellosis (undulant fever) from person to person does exist, a diligent search of the literature reveals no report of such an occurrence.

DIPHTHERIA CARRIERS

To the Editor:—In THE JOURNAL, February 5, page 461, is an inquiry regarding treatment for diphtheria carriers. In our service at Bellevue Hospital my associates and I have been called on from time to time to treat diphtheria carriers from the Municipal Contagious Disease Hospital who have been under restraint and medical care without success for long periods. We have administered roentgen therapy and it has proved successful in practically all cases. Our rationale for this treatment is based on the fact that our experience has shown that irradiation causes a fibrosis and shrinkage of tonsillar tissue. While x-rays are not in themselves bactericidal, they do favorably affect inflammatory conditions, and the endotoxins formed thereby do destroy bacteria. Therefore roentgen therapy is the proper method for destroying the foci harboring tissue of the diphtheria carrier.

IRA I. KAPLAN, M.D., New York.

BENZEDRINE AND ATROPINE AS CYCLOPLEGIC

To the Editor:—An inquiry in the February 26 issue of THE JOURNAL shows misunderstanding regarding the use of benzedrine and homatropine for refraction which might lead to disappointment. McAdams and I use benzedrine both with homatropine and with atropine when those cycloplegics are indicated. The advantage of the combination is that one instillation each of benzedrine with a cycloplegic, close together, gives approximately the same result as the conventional multiple instillations of the cycloplegic alone, with quick recovery. We do not, however, find it more efficient than prolonged atropinization, nor do we space the instillations twenty minutes apart. The report of our experience, given at the meeting of the American Academy of Ophthalmology and Otolaryngology, is found in the February issue of the *American Journal of Ophthalmology*, volume 21, page 121.

S. JUDD BEACH, M.D., Portland, Me.

KOPLIK'S SIGN

To the Editor:—On February 1 a patient came to my office with respiratory symptoms. It was necessary to diagnose at once, as a measles epidemic was prevalent. On examining the mouth for Koplik's sign of measles I projected the ultraviolet ray (quartz light) into the mouth. I found a very distinct definition of Koplik's sign, making diagnosis of measles easy. When I visited the patient two days later, the rash had made its appearance. This is apparently the first time this method of diagnosis has been used to bring Koplik's sign out clearly.

GEORGE B. HERSHEY, M.D., Gap, Pa.

Council on Medical Education and Hospitals

ANNUAL CONGRESS ON MEDICAL EDUCATION AND LICENSURE

Thirty-Fourth Annual Meeting, held in Chicago, Feb. 14 and 15, 1938

DR. RAY LYMAN WILBUR, Stanford University, Calif., in the Chair

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

FEBRUARY 14—MORNING

Report of the Council on Medical Education and Hospitals

DR. RAY LYMAN WILBUR, Stanford University, Calif.: This paper will be published in full in THE JOURNAL.

Professional Licensure

JOHN KIRKLAND CLARK, New York: One problem which the State Board of Law Examiners in New York is concerned with only most indirectly is the aptitude of the candidate for admission to the profession. This testing is conducted by separate and independent local bodies appointed by the intermediate courts of appeal in the four separate judicial departments of the state, one in New York County, one in the borough of Brooklyn (Kings County) in New York City and the others in Albany and in Rochester. While the unpaid members of the committees on character and fitness are men of high character and ability and devote much time to the problems, they, I believe, would be the first to state that the present method of handling the problem assigned them is not as effective as they would desire. Both doctors and lawyers agree that a man should not be admitted to either profession who is not fitted by personality and temperament to engage in the profession and who has not a character which will enable him to handle successfully and satisfactorily the ethical problems which are bound to confront him. It is obvious from a mere statement of the problem that a board like ours, or a group like the committees on character and fitness, cannot effectively appraise the personalities of the candidates for admission, as to their character content, with anything like the accuracy with which mental abilities can be appraised.

However accurate we have become or may become as to the appraisal of mentality, the work of professional licensure must continue to be unsatisfactory until some more successful method of appraising the character elements in personalities becomes developed into a readily applicable technic. In mental appraisals we can make use of definite types of questions—the propounding of long and intricate problems, writing of essays, the use of "true-false" or short form questions. Would that we could devise some equally efficient system for the appraisal of moral qualities!

Thus far, no such technic has been successfully developed. The opportunities afforded to those engaged in the administration of our medical schools and hospitals give your profession a much wider opportunity for personality study than is afforded to the faculties of our law schools in the appraisal of the ethical qualities of their students. In law schools, particularly in the "part time schools" from which the bulk of our candidates are derived, there is practically no opportunity for the teachers to gain more than a faint impression of even the physical and intellectual personalities of the students who attend the lectures and quizzes. We in the law greatly need the cooperation of your profession, and both professions, I feel, should much more insistently call for aid from our brothers in the general educational world in the solution of this problem. One of the essential difficulties, of course, is that in a large proportion of the cases character formation is so incomplete at the ages of 21 to 25 that an accurate appraisal of the future moral development of the candidate is difficult.

The most interesting of the methods which are being employed is that which the state of Pennsylvania has been

experimenting with. There the process of study of the character and fitness of the individual who desires to become a lawyer begins at the time he enters the law school and continues throughout his course of studies. Each prospective candidate is required to fill out a questionnaire before he begins and is assigned to a practicing lawyer as his adviser. This practicing lawyer is charged with the responsibility of interviewing the candidate from time to time during his law school course and studying his personality, his background, his associations, and his habits of living and of thinking. It seems probable that something along these lines in both professions may well be thoroughly tried out in the endeavor to obtain a more accurate method of testing ethical qualities.

This question of the extent of the existence of an ascertainable moral quality in a youth in his twenties, which quality is not at all accurately appraisable, is one which may well call for thorough psychologic study by members of your profession and by those interested in education.

There is one other subject to which I wish to refer. That is the subject of establishing certified lists of members of the medical profession qualified in the several specialties. The result of the decision of our New York Court of Appeals in the case of *Szold* v. *Outlet Embroidery Supply Co., Inc.*, 274 N. Y. 271, opens up a field for advanced professional licensure which many thought was incapable of establishment as a governmental regulation. If, by such accrediting bodies as are therein recognized, it may be possible hereafter to create a limited group of qualified specialists and confine the giving of expert testimony in court to those who establish that they have been thus licensed and accredited, one of the great scandals in which both of our professions are concerned, namely, the use of incompetent and unqualified doctors who pretend to be specialists, may be largely if not entirely ended.

The School of Medicine in the University

ALPHONSE M. SCHWITALLA, S.J., St. Louis: The significance of the professional school's integration in the university is that all the constituent elements of a professional school can have a deeper and wider background than they could possibly have if the professional school were an isolated and self-contained unit. The research function, the teaching function and the welfare function of the professional school, for example, the medical school, thus become chapters in a larger book. Research in any one of the branches of medicine should borrow increased efficacy from the fundamental sciences which are fostered by the university as a whole. The teaching function should derive from the departments of education, psychology, sociology and social work a profounder grasp of the functioning of the human mind. The dynamic function of the medical school should derive meaning from the university's philosophy, economics and public relationships. Similarly too the structural and functional elements of the medical school will derive a profounder meaning when viewed from the standpoint of and when reciprocably they contribute to the corresponding structural and functional elements of the university as a whole. The curriculum of the school of medicine should be enriched in scope by reason of the readily available knowledge in other mental disciplines. The educational methods should experience a periodic rejuvenescence; administration should be liberalized; all of the progressive thinking in practically all fields of human knowledge and experience should more promptly and effectively be placed at the disposal of the medical school for immediate absorption and assimilation. No development in the field of general education should fail in achieving an immediate influence in the school of medicine. Each trend in education which has met the test of approved experience in any particular field should not fail to leave its imprint on a modified trend in a school of medicine. There are valuable trends in our universities which have not as yet found their fullest acceptance in our professional schools. I am thinking, for example, of the splendid efforts made by our colleges of arts and sciences in the study of the individual student. The trends toward more careful selection, the study of specific traits as preparations for particular activities, the enlargement and broader concepts of personnel work, the carefully worked out principles in teacher selection, the application of well established procedures in teaching methods, the harmonization of school curriculums with school objectives—in all these, certain divisions of the universities, in some of them the schools of engineering, in others the schools of law, in others the schools of business administration, and in others the colleges of arts and sciences have outrun if not the schools of medicine as a group then certainly some schools of medicine located in the very universities in which the most profitable work has been done toward the development of new technics or new procedures, the establishment of new educational methods. Of course, I must insist that in some of our universities the school of medicine is actually in the front rank of the institution's development and is setting the pace not only for the other professional schools but also for the college of liberal arts and the graduate school. But this fact only emphasizes the need of a greater unification in the institution. I am pleading for a recognition by the medical school itself of the objective which it has to prepare physicians who will be equally prepared to practice not only in the spirit of the science but also in the spirit of the art of medicine; to prepare practitioners who will see the deeper meanings for human betterment of the work which they are preparing to do; who will be cultured gentlemen no less than keen diagnosticians, patient but forceful leaders in their communities no less than merely men who earn their livelihood by restoring the sick to health.

With reference to intra-university relationships, the school of medicine must depend on the liberal arts college to a great extent for student selection. Merely to demand a two or three years of college or even a bachelor's degree has in itself relatively little significance for the selection of a student as a student of medicine. Even the emphasis which has recently been thrown on the necessity of eliminating the so-called premedical curriculum, extremely valuable though that emphasis is and the reciprocal emphasis on the necessity of broad culture as a necessity for medicine, still misses something of the deeper inwardness of the problem. The problem is still the detection of the particular student who should be encouraged to ambition the life and the responsibilities of the medical practitioner. Every school of medicine has much to learn from and much to give to the college of liberal arts in its own university. In these fields of educational endeavor, one would welcome the closest possible communication between the faculties of medicine and the colleges, between the administrators of both institutions, between faculty committees which have related functions in their separate institutions. One would welcome equally increased efforts at promoting these relationships on the part of the higher officials of the university who are responsible for the programs of the institutions as a whole; the presidents and the members of our various university boards and committees whose interests embrace both the professional and the professional units of their respective institutions.

In view of the rapidly enlarging program in graduate medical education, the school of medicine will find itself leaning more heavily on the graduate schools of our universities. The utmost caution is here indicated. On the one hand, the graduate school if it is to serve a real function as a promotional agency, can never forget that graduate medical education has not foresworn the objectives of all medical education and that graduate medical education must contemplate the more complete development of the practitioner in a specialized field of medicine. On the other hand, the school of medicine must not and cannot forget that the future development of the specialist depends largely not only on the perfection of medical skills but also on a deepening of medical science. The efforts, therefore, of the graduate schools and of the schools of medicine must be mutually cooperative if the end result is not to be lost sight of and if medicine, and all which better medical practice means, is to achieve the function for which it has been organized. Contradictory symptoms with reference to a weakening of the desirable relationships are developing in diverse places. On the one hand we find a progressive formalizing of programs in curriculums for graduate medical education; on the other hand we find a disregard of the art of medicine on the graduate school level and unjustifiable aggrandizement on the part of medical science. On the one hand again we find didactic methods in graduate medical education which would no longer today be tolerated in the more progressive undergraduate schools of medicine and, on the other

hand, we find programs which leave the graduate student of a medical specialty so much to his own devices that his efforts at self education are the only efforts which are made and to which the institution contributes little more than the fact that the student has been registered. These contradictions are so serious because in many institutions we are just now passing through the period of origins.

No one can be sure that the graduate medical education of the future will have the same objectives as undergraduate medical education, but at least as a starting point our aim at the present moment, our aim at graduate medical education at least in the clinical sciences and arts, is to achieve in a better and more specialized manner what we have previously achieved in a general way through our undergraduate medical curriculum.

Medical education can never be unmindful of the enormous debt of gratitude which it owes to the universities. The universities have been most generous in their support of this particular professional school, mindful of the great purposes which medical education attempts to subserve. A school of medicine cannot support itself on income from students alone. The school of medicine, therefore, must in most institutions depend on the university to supplement the income derived from student fees. Different universities again support their schools of medicine with variable percentages of the total costs of the school of medicine. The financial support which the university gives to the school of medicine is an expression of the university's altruistic attitude toward its clientele, toward its student body and toward the communities which the university serve.

Factual data can be supplied to show that university influence in the school of medicine is not without its dangers. We have been accustomed to thinking of certain departments in the school of medicine, such as the department of biochemistry or of anatomy or of physiology or of bacteriology, even of the clinical departments, for example, pediatrics, internal medicine or surgery, as university departments. If the meaning of the phrase is simply this, that these departments are conceived as divisions of the university in the same sense as are the departments of Latin or of sociology or of physics, the implications may be innocent enough. If, on the other hand, the implication of a university department is that, in these various departments, students of all kinds may assemble and that student body in courses conducted by these departments may be made up of students from diverse professional groups as well as of students from the graduate school or liberal arts college, then there may be and sometimes there is considerable danger in this form of organization to the student of the school of medicine. Into a class composed of students with specific objectives and conducted by such teaching methods as I have suggested, we sometimes introduce students from other divisions of the university, from other professional schools or sometimes students of the liberal arts. I will not deny the possibility that other than medical students can profit by such administrative procedures, but my concern is largely for the diffusion of professional interest which arises from the presence in a class of a large number of other than medical students. Other examples might be chosen to illustrate the point. One might conceivably permit students of medical social service, for example, in a course on psychiatry as given to sophomores or juniors on the assumption that the medical social service student has already achieved to some extent at least an understanding of the medical point of view through a thorough course in medical essentials and especially through exposure to field work in a hospital or in an outpatient department. But to admit into a class in psychiatry as taught to medical students a group of students from the family welfare field or the child welfare field whose whole approach to a medical problem has been that of a person who regards the health problem as incidental, to allow such students to follow the technical discussions of a complicated case history seems to me to be not only an unwarranted but also an educational indefensible procedure. I am not pleading for the erection of Chinese walls around the departments of our schools of medicine. Nevertheless, in order to place better medicine at the disposal of the nation it seems essential to safeguard the processes of medical education. By all means let us extend the meaning of medical education to other groups than simply our medical students, but when we are instructing medical students and thus preparing the practitioner of medicine we can scarcely at the same time and by the same methods expect to prepare what I cannot but regard as the lay mind for the understanding of hygiene and health problems. One is an effort in professional education; the other is an effort in popular education, adult education, even though it is followed under the auspices of a graduate school.

The Functions of the Special Examining Boards

DR. WILLARD C. RAPPLEYE, New York: The recent advances in the graduate fields would not have been possible except for the phenomenal elevation of medical education in the United States since 1900 through the efforts of the Council on Medical Education and Hospitals, the foundations, the universities, the licensing bodies and private philanthropy. Graduate training has always been a well recognized part of the educational programs of leading medical schools and teaching hospitals. Present plans for the extensive development of such training to meet the need for better rather than more physicians are based largely on the long experience of teaching institutions.

In response to the desire to establish common aims within single specialties, the American Board of Ophthalmology was created in 1916 and the American Board of Otolaryngology in 1924. Other boards were organized and shortly each specialty sought a board of its own. These several developments laid the groundwork for the organization of the Advisory Board for Medical Specialties in 1933. This body was founded by representatives of the different groups of specialists and of the medical schools, hospitals and licensing bodies to coordinate the efforts of the individual boards in securing reasonable uniformity in standards and functions. The action of the House of Delegates of the American Medical Association in the same year arose from recognition of the desirability of central approval of the requirements for training in the clinical specialties.

The programs are moving forward in response to the need in every area of the country of a proper number of specialists who, in addition to a sound basic preparation, are qualified by graduate training, technical skill, judgment and experience to perform the specialized services which some patients require. It is obvious that opportunities for advanced training must be made available because the usual medical course and internship aim to provide a student only with the elementary and introductory principles of medicine. The mass of scientific knowledge and the variety of skills needed in all divisions of practice are far too extensive to be covered satisfactorily in the usual course. No phase of medical service is more important than the further training of all physicians and particularly the identification of those who wish to limit their practice to a specialty.

The primary function of each specialty board is that of promoting adequate training in its own field of practice. In the certification of specialists, each board recognizes the necessity of adapting accepted standards to meet the situation of those doctors already in practice who are partially trained in a special field and also that group of older physicians who are well recognized in their specialty. The latter constitutes the founder groups in the different fields and the former will gradually disappear as the younger graduates complete the more formal type of training which is recognized by the specialty boards as the most desirable. Other considerations include the conversion of many existing facilities into acceptable residencies. Such residencies should provide satisfactory laboratory instruction and the development of a teaching personnel in many hospitals not now engaged in an educational program. Financial aid for such projects will have to be found.

Considerable wisdom and patience must be exercised in reconciling those phases of graduate medicine which are related to the limitation of practice to a single field and those which concern the training and other qualifications of an individual to meet his responsibilities in any given specialty. Fortunately, there is wide recognition of the dangers of setting up watertight, more or less artificial compartments of practice and training. Specialized practice concerns itself with the patient as an entity quite as much as with the particular disease with which one of his organs may at the moment be involved. In discharging their functions, the boards are trying to avoid rigid rules and regulations which would even attempt to stand-

ardize practice in the different fields. They recognize that the program of graduate medicine is one of education broadly conceived and that their requirements must be kept flexible.

The unit of true education is the student, who should be given every opportunity for the development of initiative, self reliance, resourcefulness, and proper habits as well as methods of study. The plans for graduate medicine and for recognizing properly qualified specialists must be closely articulated with parallel educational programs for the general or family physician, who must provide the basic professional services in every community.

The boards must of necessity have close working relationships with hospitals, in which most of the graduate preparation must be provided. A function of the boards is to make clear to hospitals and the profession that the internship should be looked on as a part of the basic training of a student and that it should not be regarded as advanced equipment for the practice of a specialty. The boards must function in close relationship to the licensing bodies in the different states. There is abundant evidence that the functions of the boards of specialists are only a part of the larger plan of medical education. It is highly important that these functions be harmonized with the developments and needs of the other parts of the educational scheme. The premedical student, the medical student, the intern, the resident, the general practitioner, the specialist, the teacher, the investigator and the public health administrator should be regarded from an educational point of view merely as different phases of the training of personnel to meet the health needs of the country. The problems from college preparation to retirement from professional life should be looked on broadly as parts of a single educational program. Some of these parts are primarily within the jurisdiction of universities, some are largely within the domain of the hospitals, others are in the various fields of practice, and some are under direct governmental regulations.

There is urgent need for coordination of the various subdivisions of medical education and for better definition of the several areas of responsibility of national and state agencies, universities, hospitals and professional bodies dealing with portions of the whole program, if medicine in this country is to meet fully its obligations.

DISCUSSION

DR. WALTER L. BIERRING, Des Moines, Iowa: I wish to relate my remarks to the paper of Dr. Rappleye, who has brought out the relation between the training of the specialist and graduate education. There is no doubt that the time which will be required for this specialized training will vary and will be determined more in the years to come. There is a feeling that specialized practice should not be entered until at least ten years has transpired from the time of graduation or the completion of a hospital intern year. Special training belongs in the field of graduate education, but it is hoped that in standardizing or in outlining a course of study it may not be strictly confined to a certain quota of hours or specific curriculum, but that there may be even more elective privileges than are now being developed in undergraduate curriculums. It has been the experience of one of the examining boards or the method that has been devised by them, that of internal medicine, of not in any way particularly indicating the institution or the course of study but depending largely on the individual himself, placing the responsibility of the training on the individual concerned, whether it is in this country or in a foreign country, in a small or a large institution; that is his responsibility. The determination of the qualifications of the individual for the specialty he wishes to practice lies entirely with the particular certifying board. It is the responsibility of the board to determine whether that training is adequate for his being certified in that specialty.

DR. BURT R. SHURLY, Detroit: With an experience of fourteen years on a special examining board during which we have examined more than 2,500 men and the number of failures has been some 20 per cent, and as one particularly interested in originating the Advisory Board for Medical Specialties, it seems to me it is time to lay out a definite program that will have to it a vision and a far-reaching plan throughout this country to furnish sufficient opportunity in graduate training for these various specialties. I have felt through these years that the pendulum has been swinging so rapidly in medicine that we err many times in our enthusiasm by being carried away into a field that becomes much too limited. The spirit of liberalism in education must come back, so that we recognize the true value of basic general surgery and general internal medicine. While we have these numerous societies and numerous boards and numerous governmental controls, it seems to me that some of those should be eliminated. In Wayne University we have developed a course for all interns in all hospitals of the city of Detroit, where they may have a splendid course in anatomy and pathology, which we find are the two weak subjects as these men come up before us for examination. While we have in otolaryngology only 150 vacancies throughout the year, there are still inadequate training grounds for those men, and that certainly must be developed in each of these special boards.

(To be continued)

Medical Examinations and Licensure

COMING EXAMINATIONS

STATE AND TERRITORIAL BOARDS

ALABAMA: Montgomery, June 28. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ARIZONA: Phoenix, April 5-6. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS: *Basic Science.* Little Rock, June 4. Sec., Mr. Louis E. Gebauer, 701 Main St., Little Rock. *Medical (Regular).* Little Rock, June 21-22. Sec., State Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Medical (Eclectic).* Little Rock, June 21. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Reciprocity.* San Francisco, May 11, Los Angeles, July 11, San Francisco, Sept. 14, and Los Angeles, Nov. 16. *Written examinations.* San Francisco, June 27-30, Los Angeles, July 11-14, and Sacramento, Oct. 17-20. Sec., Dr. Charles B. Pinkham, 420 State Office Bldg., Sacramento.

COLORADO: Denver, April 6-8. Sec., Dr. Harvey W. Snyder, 831 Republic Bldg., Denver.

CONNECTICUT: *Basic Science.* New Haven, June 11. *Prerequisite to license examination.* Address State Board of Healing Arts, 1895 Yale Station, New Haven.

DELAWARE: Dover, July 12-14. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: *Basic Science.* Washington, June 27-28. *Medical.* Washington, July 11-12. Asst. Sec., Commission on Licensure, Mr. Paul Foley, 203 District Bldg., Washington.

FLORIDA: Jacksonville, June 13-14. Sec., Dr. William M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, June. Joint Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, April 11-14. Sec., Dr. James A. Morgan, 48 Alexander Young Bldg., Honolulu.

IDAHO: Boise, April 5-6. Commissioner of Law Enforcement, Hon. J. L. Balderston, 205 State Capitol Bldg., Boise.

ILLINOIS: Chicago, April 5-7, June 28-July 1, and Oct. 18-20. Superintendent of Registration, Department of Registration and Education, Mr. Homer J. Byrd, Springfield.

INDIANA: Indianapolis, June 21-23. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, 301 State House, Indianapolis.

KANSAS: Kansas City, June 7-8. Sec., Board of Medical Registration and Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: Louisville, June 8-10. Sec., State Board of Health, Dr. A. T. McCormack, 620 S. 3rd St., Louisville.

MARYLAND: *Medical (Regular).* Baltimore, June 21-24. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Medical (Homeopathic).* Baltimore, June 21-22. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MICHIGAN: Ann Arbor and Detroit, June 13-15. Sec., Board of Registration in Medicine, Dr. J. Earl McIntyre, 202-3-4 Hollister Bldg., Lansing.

MINNESOTA: *Basic Science.* Minneapolis, April 5-6. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis. *Medical.* Minneapolis, April 19-21. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: Jackson, June. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MONTANA: Helena, April 5-6. Sec., Dr. S. A. Cooney, 205 Power Block, Helena.

NEBRASKA: *Basic Science.* Omaha, May 3-4. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, State House, Lincoln.

NEVADA: Carson City, May 2. Sec., Dr. John E. Worden, Capitol Bldg., Carson City.

NEW JERSEY: Trenton, June 21-22. Sec., Dr. James J. McGuire, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, April 11-12. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NEW YORK: Albany, Buffalo, New York, and Syracuse, June 27-30 and Sept. 19-22. Chief, Professional Examinations Bureau, Mr. Herbert J. Hamilton, 315 Education Bldg., Albany.

NORTH CAROLINA: Raleigh, June 13. Sec., Dr. B. J. Lawrence, 503 Professional Bldg., Raleigh.

NORTH DAKOTA: Grand Forks, July 5-8. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.

OKLAHOMA: *Basic Science.* Oklahoma City, May 4. Sec. of State, Hon. Frank C. Carter, State Capitol Bldg., Oklahoma City. *Medical.* Oklahoma City, June 8-9. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: *Basic Science:* Corvallis, July 16, and Portland, Nov. 19. Sec., State Board of Higher Education, Mr. Charles D. Byrne, University of Oregon, Eugene. *Medical. Reciprocity.* Portland, April 6. Sec., Dr. Joseph F. Wood, 509 Selling Bldg., Portland.

PENNSYLVANIA: Philadelphia and Pittsburgh, July. Sec., Board of Medical Education and Licensure, Dr. James A. Newpher, 400 Education Bldg., Harrisburg.

RHODE ISLAND: Providence, April 7-8. Chief, Division of Examiners, Mr. Robert D. Wholey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, June 28. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: July 19-20. Director of Medical Licensure, Dr. B. A. Dyar, State Board of Health, Pierre.

TEXAS: San Antonio, June 20-22. Sec., Dr. T. J. Crowe, 918 Mercantile Bldg., Dallas.

VERMONT: Burlington, June 15-17. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, June 22-24. Sec., Dr. J. W. Preston, 30½ Franklin Road, Roanoke.

WISCONSIN: Milwaukee, June 28-July 1. Sec., Dr. Henry J. Gramling, 2203 S. Layton Blvd., Milwaukee.

WYOMING: Cheyenne, June. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

NATIONAL BOARD OF MEDICAL EXAMINERS SPECIAL BOARDS

Examinations of the *National Board of Medical Examiners* and *Special Boards* were published in THE JOURNAL, March 26, page 1060.

Mississippi Reciprocity Report

Dr. R. N. Whitfield, assistant secretary, Mississippi State Board of Health, reports 8 physicians licensed by reciprocity at the meeting held in Jackson, Dec. 8, 1937. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
Hahnemann Medical College and Hospital, Chicago		(1907)	Illinois
Tulane University of Louisiana School of Medicine		(1936)	Louisiana
Tufts College Medical School		(1930)	Mass.
Creighton University School of Medicine		(1927)	Nebraska
Jefferson Medical College of Philadelphia		(1898)	R. Island
University of Tennessee College of Medicine		(1934), (1935), (1936)	Tennessee

Indiana Reciprocity and Endorsement Report

Dr. J. W. Bowers, secretary, Indiana State Board of Medical Registration and Examination, reports 54 physicians licensed by reciprocity and three physicians licensed by endorsement during 1937. The following schools were represented:

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Arkansas School of Medicine		(1933), (1935, 2)	Arkansas
Stanford University School of Medicine		(1936)	California
University of Colorado School of Medicine		(1934)	Maryland
Howard University College of Medicine		(1935)	Missouri
Emory University School of Medicine		(1931), (1935)	Georgia
Chicago College of Medicine and Surgery		(1911), (1912)	Illinois
Loyola University School of Medicine		(1928), (1931)	Illinois
Northwestern University Medical School		(1935)	Illinois
Rush Medical College		(1929), (1933), (1934), (1936, 2)	Illinois (1936) Michigan
School of Medicine of the Division of the Biological Sciences		(1934)	Illinois
University of Illinois College of Medicine		(1916)	Illinois
Indiana University School of Medicine		(1928)	Penna.
University of Kansas School of Medicine		(1932)	Kansas
University of Louisville School of Medicine		(1924), (1933), (1935, 3)	Kentucky
Tulane University of Louisiana School of Medicine		(1919)	Louisiana
University of Maryland School of Medicine and College of Physicians and Surgeons		(1932)	Maryland
University of Michigan Medical School		(1925), (1930), (1931), (1932)	Michigan
St. Louis University School of Medicine		(1934)	Missouri
Washington University School of Medicine		(1934), (1935, 2)	Missouri
Ohio State University College of Medicine		(1935, 2), (1936)	Ohio
Western Reserve Univ. School of Medicine		(1934), (1936)	Ohio
Temple University School of Medicine		(1927)	Penna.
University of Pennsylvania School of Medicine		(1928)	Wisconsin, (1930) Pennsylvania
University of Pittsburgh School of Medicine		(1928), (1932)	Penna.
Meharry Medical College		(1936)	Tennessee
University of Tennessee College of Medicine		(1934)	Tennessee
Marquette University School of Medicine		(1936)	Wisconsin, (1937) Michigan
Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin		(1933)	Illinois
Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest		(1923)	Illinois

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
University of Colorado School of Medicine		(1934)	N. B. M. Ex.
Rush Medical College		(1928)	N. B. M. Ex.
Washington University School of Medicine		(1930)	N. B. M. Ex.

Book Notices

Pathology of the Central Nervous System: A Study Based upon a Survey of Lesions Found in a Series of Fifteen Thousand Autopsies. By Cyril B. Courville, M.D., Professor of Neurology and Psychiatry, College of Medical Evangelists, Los Angeles. Cloth. Price, $5.75 Pp. 344, with 200 illustrations. Mountain View, California: Pacific Press Publishing Association, 1937.

The present volume is an excellent work devoted mainly to the gross pathology of the brain and the nervous system. The author has studied fifteen thousand brains and spinal cords post mortem, twelve thousand of which came under his personal observation. From this vast amount of material he has organized a textbook which covers thoroughly the innumerable descriptive phases of his cases. The work follows, in general, classifications set up clinically. Part one is devoted to congenital anomalies and malformations, part two to diseases of the intracranial blood vessels, part three to infectious diseases of the central nervous system, part four to the effects of trauma, part five to intoxications, part six to diseases of unknown etiology and part seven to tumors of the intracranial and intraspinal spaces. Little case history material is given on individual cases and the microscopic details are largely left for some one else's discussion, but each one of the major pathologic conditions found in the brain and spinal cord—the former in particular—is covered in some detail, particularly in relation to the gross appearance and the circumstances of causation. In spite of the vast amount of case material studied, statistical information about anomalies, peculiar variations, numbers of cases of rare entities and other rather obscure phases are not treated very thoroughly, but nevertheless the material in the book does not seem to be duplicated elsewhere in the specific form in which it appears here. For each condition one finds one or more excellent photographic reproductions showing the exact appearance of the organ and, in some cases, showing the gross tissue changes. A number of beautifully executed drawings illustrate the clinical point under discussion and anatomic features in connection with the pathologic entities, but the text does not devote itself very much to clinical observations, physiology or obscure disorders. Special attention must be drawn to the appendix, in which the author lists a number of clinicopathologic aphorisms which seem to be, on the whole, true and are rather pithily presented. Many of them direct the student's attention to obscure pathologic conditions that might be neglected. Others offer general rules which might well be remembered in all cases dealing with disorders of the nervous system. This book is well written, has been carefully edited, and would satisfy a need for both the neuropathologist and the clinical neurologist who desires something between the general clinical neurologic textbook and the usual microneuropathologic work.

La vie médicale aux XVI^e^, XVII^e^ et XVIII^e^ siècles. Par le Docteur Paul Delaunay, membre de la Société française d'histoire de la médecine. Paper. Price, 40 francs. Pp. 556, with 114 illustrations. Paris: Le François, 1935.

Professor Delaunay's Vie médicale is a splendid addition to this series in the historical field. It is limited in its scope to French medicine and excludes surgery because of the medieval schism between medicine and surgery, which continued in France, though not in Italy, when the physicus became a medicus. The work treats of the life of the medical student and of the private, professional, corporative, religious, political, social, intellectual and doctrinal life of the full fledged and active *médecin.* The text is amply documented with citations of authorities and finely illustrated with well selected reproductions from contemporary prints, portraits, engravings and paintings. It thus affords a detailed and accurate picture of the preparation and professional activities of the physician in France and his wide cultural relations from the opening of the sixteenth century up to the close of the eighteenth. The Faculty of Medicine was established at Montpelier in 1220 A. D., giving stability, continuity, wider influence and permanent privileges to medical education. A federation of teachers under the egis of the chancellor of Notre Dame opened formal instruction in Paris. Chairs of medicine multiplied as the universities were organized in the thirteenth to the sixteenth centuries until

students had a wide field from which to choose. It was the custom for medical students to migrate from school to school even across national boundaries. Vesalius began his studies in Belgium, went to Montpelier and to Paris, reentered Louvain, took his bonnet at Basle, and taught at Padua. This academic dromomania had its origin in the international character of learning, the inequalities in instruction, the transfers of teachers and the wanderlust of youth. Religious turmoil accompanying the Reformation scattered pupils and teachers, and the epidemics of plague repeatedly decimated and scattered both students and faculties. At Montpelier in 1527 the students were taxed at the "anatomy" for gratuities to the watchman who brought the body, to his wife who furnished the linen, to porters, washers, interpreter, prosector, beadle and janitress and her children who ran errands, to say nothing of charges for wine, for washing, vessels for viscera, incense, fuel and candles. Library facilities were meager. In 1527 Montpelier had fifty volumes. Books were chained to keep them and fees were charged for their use. Catalogues emerged to prevent losses. Herborizations took students afield and tickets admitted them to botanic gardens of medicinal herbs. The family life of the physician, his office, furniture, library, costume, bedside manners, remuneration, professional ethics, relations with apothecaries, patients, the nobility and the court are all passed in review. The author reviews the contributions of the profession to the intellectual life of these three centuries, tracing the decline of humanism; their contributions to anatomy, physiology, botany, zoology, physics and agriculture; their share in the formation of academies and learned societies, and their aid in forwarding scientific publication and establishing high standards of scientific work. He traces the changes in medical doctrine from wreckage of the galenic school to the organized knowledge of the encyclopedists. This scholarly treatise is an epitome of the history of medicine in the formative centuries during which the arts and science of medicine emerged from scholasticism, superstition and charlatinism into the clearer light of the dawning modern period.

Operative Obstetrics: A Guide to the Difficulties and Complications of Obstetric Practice. By J. M. Munro Kerr, LL.D., M.D., F.C.O.G., Obstetric Surgeon, Glasgow Maternity Hospital, Glasgow. Fourth edition. With the assistance of Donald McIntyre, M.D., F.C.O.G., Consulting Obstetric Surgeon, Barshaw Maternity Hospital, Glasgow, and D. Fyfe Anderson, M.D., Senior Assistant to Professor of Obstetrics and Gynæcology (Muirhead Chair) Glasgow University. Cloth. Price, $12. Pp. 847, with 338 illustrations. Baltimore: William Wood & Company, 1937.

The fourth edition of this noted work, previously entitled "Operative Midwifery," has been brought down to date by thorough revision and rewriting. In this task Dr. Kerr acknowledges the assistance rendered by Donald McIntyre and D. Fyfe Anderson, who have collaborated with him in this new edition. The book is unique in that it deals only with those phases of obstetric practice which require operative intervention. Other abnormalities, such as toxemias of pregnancy and, logically, the normal aspects of obstetrics, are completely omitted. Kerr calls attention to the fact that in England, as in America, maternal and fetal mortality and morbidity are unnecessarily high, emphasizing that the knowledge of when and how to intervene is of paramount importance. His opening paragraph is an essay in itself:

> Nature in parturition, although generally following a certain course, refuses to be trammeled by hard and fast rules. It is important for the accoucheur to remember this, and to appreciate within what limits Nature may be allowed a free hand. The mistake is too often made of forgetting this and of interfering, when, with a little patience, it would have been unnecessary. But, if it is of importance that the accoucheur should appreciate the natural variations of parturition, it is equally important that he should recognize when nature is at fault, and that he should do this as early as possible. *He must never presume that a parturition is normal. He must not be content until he has satisfied himself that it is not abnormal.* Again and again one sees how failure in this respect results in complications being overlooked until they cannot be remedied, and the child's and even occasionally the mother's, life sacrificed or greatly endangered. This does not imply that he must always interfere early in labour; in many cases of dystocia *timing* of interference is the all important detail.

In general there is little but still some difference between obstetric practice in this country and that advocated by Kerr. He discusses the importance of antepartum care, even though it has not yet succeeded in materially lowering the death rate, saying it has not had a "fair deal." He speaks of a complete examination in the thirty-fourth to thirty-sixth week to discover abnormalities and to anticipate dystocia. By this he does not mean to indicate that no earlier routine care is necessary though he fails to specify this. From his writings and those of other English obstetricians it often seems to appear that the pregnant women in England have not been generally taught to present themselves for antepartum care as early in pregnancy as do the women in this country.

American obstetricians will probably disagree with Kerr's advocacy of amniography, or the injection of an opaque medium, through the abdominal and uterine walls into the uterine cavity for the purpose of x-ray visualization. This is proposed by him for diagnosis of placenta praevia in doubtful instances. He finds it necessary still to argue for the use of rubber gloves; he urges more general masking of attendants on patients in labor and during the early puerperium; he favors the use of vaginal antiseptics during labor; unlike many British obstetricians, he prefers the dorsal position for delivery. Kerr utilizes the lateral type of episiotomy on occasion but considers episiotomy "seldom necessary." These various points of view, with others, are cited because they cannot fail to be of interest to those of us on this continent who will wish to compare our procedures with his.

He favors traction on the umbilical cord for delivery of the retained but detached placenta, making certain, however, by placing a marker on the cord at the vulva that the placenta has first become detached. This marker must have advanced before he permits traction, but when advancement has occurred he favors this in preference to any considerable amount of pressure over the fundus. He does not approve of attempts at manual or instrumental rotation in occipitoposterior presentations. While he still advocates the use of pubiotomy (hebosteotomy) under certain circumstances, he fails to recommend it in impacted face presentation with the chin posterior, stating that in this situation there "is no option but craniotomy even if the child be living." He favors forceps delivery of the aftercoming head in breech deliveries; he cautions wisely against the dangers of Kristeller expression during ordinary deliveries.

The chapter on contracted pelvis is excellent, the old dimensional classification being retained but with generous reference to the work of Caldwell and Moloy, Thoms, and Jarcho. He appreciates the value of the x-rays in the diagnosis of contracted pelvis but, like the experienced obstetrician that he is, states that trial of labor is more important in borderline cases. The various roentgenograms in the book are splendidly clear, but the other illustrations are for the most part simple line drawings, not at all comparable to the excellence of the text. The book is not firmly or securely bound, but the paper and printing are of fine quality. This volume should be especially helpful to the obstetric specialist and of great value to the practitioner doing obstetric work.

Innere Sekretion und Chirurgie. Von Hans Hanke, Dr. med. habil., Dozent für Chirurgie an der Universität Freiburg im Breisgau. Paper. Price, 24 marks. Pp. 326, with 18 illustrations. Berlin: Julius Springer, 1937.

The study of internal secretions appears to hold out as great a promise for medicine as did bacteriology sixty years ago. The acquisitions to medical knowledge which have come through investigation of the glands of internal secretion have been numerous. It may seem a bit odd that a surgeon would essay to encompass this somewhat strange field in a monograph. Yet, as the author points out, the surgeon was among the first of medical practitioners to concern himself over endocrinology. Through the first unhappy experiences of surgeons with the removal of goiters, much was learned concerning the behavior of the thyroid and parathyroid glands. The continued activity of surgeons in the romantic field of the endocrines has augmented medical knowledge with relation to the pituitary, the parathyroid, the pancreas and the adrenal glands. In this sound and substantial monograph the author has collected much useful information. The subject matter treated consists of the thyroid, the parathyroids, the thymus, the insular apparatus of the pancreas, the adrenal, the hypophysis, the pineal body and the sex glands. The important features of minute anatomy of the various glands are related. Then follows generally a complete discussion of the accepted and debatable physiologic functions

together with mention of the relation of the gland under discussion to other glands of internal secretion. A discussion of diseases affecting the gland and the role of surgery in treatment completes each chapter. A few more well selected illustrations would have added much to the text. The author shares apparently the attitude, heard more commonly in Europe than on the American continent, that the presence of a goiter sensitizes a patient to iodine. American students of the goiter problem will no doubt attribute this reaction in part to a prejudice which still survives from the so-called jod-Basedow (iodine hyperthyroidism) described by Kocher in 1910. It seems somewhat strange to learn (p. 206) that only two patients with hyperinsulinism had been operated on successfully in Germany up to the publication of this monograph. The author, though recognizing the relationship of the hypophysis to the normal descent of the testis, is not nearly as enthusiastic over the accomplishment of antuitrin-S in the treatment of failure of testicular descent as are many American writers. Much encouragement for the success of hypophysis transplants is offered in the reports of Sauerbruch and Kylin (p. 277), who observed startling improvement in Simmonds' disease (hypophysial cachexia) following implantation of hypophysial tissue from the calf. The results of other glandular transplantation, whether heterografts or homografts, are not good, as is admitted by the author. This splendid monograph deserves to be read and studied widely. There is much to commend and little to criticize in the volume. It can be enthusiastically recommended not only to surgeons but to any one who seeks authoritative information on the physiologic mechanisms of the glands of internal secretion.

Mental Therapy: Studies in Fifty Cases. By Louis S. London, M.D., Medical Officer, United States Veterans Bureau. Volumes I and II. Cloth. Price, $12.50 per set. Pp. 427; 428-774, with 22 illustrations. New York: Covici-Friede, 1937.

This is a rather extensive psychoanalytic work consisting of analyses of fifty individual cases, the majority of which were treated by the author and all of which were studied in his practice. The author scarcely can be considered an orthodox psychoanalyst. While many of his explanations fall definitely under the freudian egis, he does not use, as a general rule, the technic of freudian psychoanalysis. Instead, he uses the method developed by Stekel, which consists of a greater use of interpretation of and explaining to the subject the basis of his mechanisms rather than allowing him to come on it of his own accord by the use of uncontrolled association. While the basic theories behind the two types of psychoanalysis are almost identical, the explanation of the mechanism in some of London's cases would probably not elicit a hearty corroboration from the orthodox analyst. Nevertheless, there is in this volume much material that is interesting. Each case is presented in some detail, although not as completely as one usually finds in a study of psychoanalytic material. Each case, too, is designed to represent the particular type of deviation, such as a cardiac neurosis, a gastric neurosis, an anxiety neurosis, sexual impotence, sadism, masochism, schizophrenia or manic-depressive psychosis of various types. The author's descriptions of the psychotic behavior and the everyday life of the neurotic individual are meager. Much stress is laid on the symptomatic difficulties and the chief complaint. A history is given in each case showing the background, the medical observations, relationship to the parents, early sexual history and some dream material which would tend to explain the dynamism involved in the particular deviation. Each case is concluded with a comment which is rather too terse to be completely significant. The cases unfortunately are not clear cut. The psychiatrist who wishes to enlarge his horizon and to understand the dynamics of behavior to a greater extent will be sadly disappointed in the present work. While certain dynamisms are mentioned by name, and dreams may be interpreted to point out the associational machinery involved and possibly the complex material lying behind them, one cannot see the logical connections between the material and its evaluation. This is particularly true in the volume which deals with the psychoses. One is not convinced that the patients were suffering from a psychosis in the first place, and in those cases in which there seems to have been a favorable result from the author's treatment the manner in which it was brought about is not at all clear. As a matter of fact, although the author implies and of course the title indicates that the book is to be devoted to the therapeutic aspects of the cases, the only treatment apparent from the way these cases are written up is the fact that an analysis was undertaken, the dreams were analyzed, and the patient was given some insight into his mechanisms. How these were carried out is not described. There should be a detailed explanation of what technics were used, at what time, what particular features were stressed, how exactly insight was brought to the patient, and what the results of the various stages of treatment proved themselves to be as the case proceeded under the author's care. There is a great deal of dogma and little explanation. As a gesture to indicate that treatment is necessary in psychiatry and as a suggestion that conditions of widely diverse nature might be subjected to various kinds of treatment, the book has value. As a guide to treatment for the use of "psychologist, neurologist, psychiatrist, and the general practitioner, who will find the cases presented of decided value in their practice," its importance is doubtful.

Emotional Hygiene: The Art of Understanding. By Camilla M. Anderson, A.B., M.D., Assistant Professor of Nursing Education, Duquesne University, Pittsburgh. Cloth. Price, $2. Pp. 242, with illustrations by Dorothy G. Stevenson. New York & London: J. B. Lippincott Company, 1937.

The rather popular presentation of this book with its subtitle "The Art of Understanding" makes one suspect that this is another one of those superficial works devoted to telling a patient how to cure himself without a doctor or how to adjust all the problems in his life. On reading it, however, one immediately notes that the language is extremely easy to comprehend and it proves to be a small but substantial volume full of excellent factual material which well deserves perusal. It consists of three parts: The first one is devoted to a rather general and perhaps superficial presentation of mental mechanisms, with a simple explanation of behavior and a description of personality types, emotional patterns, escape mechanisms and similar features in the biologic and other bases of the behavior pattern. This part is short and rather generalized but accurate. The second part is devoted to specific discussions of how to meet problems arising from personal problems, in dealing with patients, relatives, colleagues and the environment in general. The third part is a discussion of various phases of nursing, leading one to believe that the book is primarily intended for nurses, since the author is an instructor in nursing education. The introduction does not make this clear, although the style is pointed definitely in the feminine reader group. There are many chuckles and pert illustrations, both verbal and pictorial, and practical cases are taken up and discussed in an intelligent manner. This is one of the few books on mental hygiene sufficiently well written and widely enough applicable so that it might be given to the interested reader without medical training who requests a book on this subject.

Radiation Therapy: Its Use in the Treatment of Benign and Malignant Conditions. By Ira I. Kaplan, B.Sc., M.D., Clinical Professor of Surgery, New York University Medical College. Cloth. Price, $10. Pp. 558, with 198 illustrations. New York: Oxford University Press, 1937.

The volume opens with a short survey of the historical development of radiation therapy, including radium and x-rays, the physics of x-rays and radium, descriptions of types of apparatus for the production of x-rays and their measurement, and the use of electric currents as a substitute for scalpel surgery in cutting and coagulating tissues. There then follows a chapter on irradiation in dermatology, which includes the treatment of infectious diseases of the skin and of superficial neoplasms. The remainder of the volume deals with the irradiation of tumors, the classification being based on a regional arrangement, the tumors in each organ or tissue being taken up separately. Extensive bibliographies are attached to each chapter, and the different types of tumors in different situations are copiously illustrated with photographic reproductions of the patients and photomicrographs of the tumors.

The volume contains an immense amount of useful information in compact form, but in the effort to cover the vast field a dogmatic type of presentation has been assumed which would lead the reader to think that radiation therapy has a far greater value than it really possesses and that it can be put on a prescription basis. There is a great deal of repetition in which

it is definitely stated that the radiation should be given at such and such a voltage with such and such filtration, which might lead the uninitiated to believe that all that is necessary is to apply this radiation in order to get good results. There is already too much of this routine application of x-rays to a vast number of conditions in which little or no benefit is actually obtained by such irradiation and therefore the book is dangerous for the beginner, who may be led to think that he can obtain results which the expert knows are rarely seen. It would have been much wiser had the volume covered less ground and the limited fields in which radium and x-rays are effective considered in greater detail.

There are also evidences on almost every page of haste in preparation, and numerous misspellings have been found, with misprints and the use of incorrect expressions. As an illustration of the latter, it may be a comfort to know that "females are rarely involved with lip cancer," and the phrase might well have been omitted as not illuminating the subject of cancer of the lip to any extent. An example of excessive optimism is the statement that nausea or vomiting occurring after x-ray treatments can be controlled by citric acid fruit juices or small doses of sodium bicarbonate. The author knows perfectly well, for he mentions the fact in another place, that in a certain proportion of cases nothing controls the nausea or vomiting and that treatment may have to be abandoned because of this fact. Speaking of melanomas, the author says that when metastatic lesions of the lung are present the whole chest is treated with high voltage x-rays, daily doses of 150 roentgens being given to each area alternately until a total of from 1,500 to 2,000 roentgens has been given to each area. The beginner may assume from such a statement that such irradiation is of benefit, but unfortunately the reverse is true. Speaking of mixed tumors of the salivary glands the statement is made that they do not metastasize, that the "gland" must be completely excised and that as soon as the wound is healed radiation should be administered. There are some who think that, since these tumors frequently recur locally, the tissues should not be damaged by radiation of 2,000 roentgens as recommended but should be reserved for further surgical treatment, which is often effective.

Perhaps these criticisms seem unimportant, but there is no satisfactory modern book on the subject of radiation therapy, and it is to be hoped that a prompt and thorough revision of this text along the lines indicated will be made so that the author's wide experience and judgment may be available to the large number of radiotherapists who are attempting with insufficient experience to treat patients with malignant disease for whom radiation is the only hope.

Porphyrine und Porphyrinkrankheiten. Von Priv.Doz. Dr. A. Vannotti, Sekundärarzt der Medizin, Universitätsklinik Bern. Paper. Price, 27 marks. Pp. 286, with 64 illustrations. Berlin: Julius Springer, 1937.

It is probable that the total occurrence of cases of true porphyria congenita in Europe and the United States since Günther's paper in 1911 is less than the number of papers that have been written on the subject. In the last decade, however, it has been gradually recognized that the porphyrins are of more significance to medicine than association with some pathologic curiosities. Porphyrins are fundamental components of the hemoglobins and at least some of the oxidation catalysts (cytochrome C) as well as of the chlorophylls. The brilliant chemical studies of Hans Fischer and the spectroscopic work of Dhéré have not escaped the attention of clinical investigators, especially in Germany, who are studying porphyrin metabolism in a wide variety of conditions. Reviews on the clinical significance of the porphyrins have been published recently by J. T. Brugsch (*Ergebn. d. ges. Med.* **20**:423, 1935; *Ergebn. d. inn. Med. u. Kinderh.* **51**:86, 1936). The present book by Vannotti covers clinical questions in detail in addition to voluminous literature on spectroscopy of the porphyrins, the results of experimental administration of porphyrins to both animals and man, the relation between porphyrins and iron metabolism, and general studies on porphyrins in plants, animals and bacterial cultures. The chief criticism of Vannotti's book is on the score of omission. One could wish for a more thorough treatment of the chemistry of the several porphyrins, as this is fundamental to an understanding of the clinical questions. The omission of a detailed discussion of the "HCl number" and differential solubilities of the porphyrins will be regretted by investigators who are concerned with separation and quantitative estimation of the various porphyrins in biologic materials. The nine page section on methods for estimation of the porphyrins is only a brief introduction to these complicated questions. Vannotti repeats the familiar dictum about the role of porphyrins in photosensitization, but it should be mentioned that recent studies by Blum and Pace (*Brit. J. Dermat. & Syph.* **49**:465 [Nov.] 1937) fail to confirm any general relation of porphyrins to hydroa and similar lesions resulting from light sensitivity. Studies on patients at the Mayo Clinic in 1936-1937 by Brugsch, Keys and Brunsting yielded the result that light sensitivity did not occur in any of the observed cases of moderate porphyria and that in none of the observed cases of light sensitivity was there any appreciable disturbance in porphyrin metabolism. Vannotti's book is well organized and shows, in the discussions, the understanding that comes only from having personal experience in a field of study for some years. The book should be useful to all who are interested in pigments and their metabolism; it will be indispensable to students of the porphyrins. It is unfortunate that there is as yet no work in English of comparable scope.

The Management of the Pneumonias for Physicians and Medical Students. By Jesse G. M. Bullowa, B.A., M.D., Clinical Professor of Medicine, New York University College of Medicine, New York. Cloth. Price, $8.50. Pp. 508, with 142 illustrations. New York: Oxford University Press, 1937.

Dr. Bullowa's book includes almost all phases of pneumonia except pathology. He begins with classification of the pneumonias and then gives an account of the clinical picture, the laboratory, physical and x-ray examination and the various forms of treatment. The data which he presents are drawn largely from his own extensive clinical experience at the Harlem Hospital. The book is by no means evenly written. The best chapters, those on laboratory examination and serum therapy, are evidently subjects with which he is most competent to deal. Unfortunately the author feels called on to make comments now and then on immune processes in pneumonia, a subject with which he is evidently unfamiliar, as many of his statements are misleading and others have no foundation in known fact. For instance, he states that among the factors which control invasion of the blood stream by the pneumococcus are bacteriolysins in the serum and the pneumococcidal action of the blood platelets. Evidence does not exist for either one of these two antipneumococcic activities of the blood. The chapter on oxygen therapy is much too detailed and theoretical for the clinician who wants to know the best method of giving oxygen, its indications and what can be expected from its use. Likewise, many of the charts are too complex. Even after considerable study one is not always sure of their significance. The bibliographies at the end of the chapters give the impression of being thrown together without any order and do not always include the most important contributions to the subject. In spite of its defects the book contains a great deal of valuable information and presents for the first time a collected account of the specific pneumonias caused by the different types of pneumococci I to XXIX. The author's observations on the results of the newly developed antipneumococcus rabbit serum are of particular value in view of the probable availability of this therapeutic agent in the near future.

The Family in Health and in Illness. By Florence Brown Sherbon, A.M., M.D., Professor of Child Development and Health of the Family, Department of Home Economics, University of Kansas. Cloth. Price, $3.50. Pp. 516, with 200 illustrations. New York & London: McGraw-Hill Book Company, Inc., 1937.

This book, prepared primarily for college students but with the purpose of continued usefulness after graduation, is a household manual of health and disease, containing much useful reference material but with certain glaring defects. It attempts too much in some instances, with the result that its treatment of certain topics is inadequate, and it contains statements with which many physicians will disagree. For example, the routine use of commercial mouth washes is said to be "commended as a routine habit." By whom other than the manufacturers? Sulfanilamide gets a paragraph; this is either too much space

in such a book or too little, especially when it includes the following invitation to self medication: "Sulfanilimide is effective when taken by mouth and does not produce marked physical reaction." Descriptions of the uses of procaine, ephedrine and epinephrine in one sentence as drugs which are used "to shrink the congested membranes and open up the breathing passages" are out of place in such a book, even when followed by the warning "Novocain and adrenalin should never be used except by a physician, and ephedrine should not be used continuously or in chronic conditions except under a physician's advice." If that is so, why should they be mentioned here at all, especially in terms which first seem to recommend, then condemn? The only result, as any physician should realize, will be to stimulate attempts at self medication, despite warnings against it appearing elsewhere in the book. For the most part the book is serviceable, except that efforts to be brief often make the discussions, especially of the specific diseases, unsatisfactory, as for example this sentence from the description of pernicious anemia: "Absence of gastric acid and spinal cord paralyses is usually noted in some degree and is almost a specific symptom." Aside from the faulty sentence construction, which might lead the inexperienced reader to infer that "absence of . . . spinal cord paralysis is almost a specific symptom," whereas the reverse is meant, this information is of absolutely no use to the reader of such a manual, especially when this is almost all there is on symptomatology of this disease. Moreover, false hope is held out for prevention of pernicious anemia in the statement that it "consists in pursuing a 'balanced' mode of life especially with reference to a diet containing a full amount of vitamins and minerals." Such questionable passages greatly impair the value of a book that contains much useful information. How is the untrained reader going to separate the wheat from the chaff?

Illustrations of Regional Anatomy. By E. B. Jamieson, M.D., Senior Demonstrator and Lecturer, Anatomy Department, University, Edinburgh. Section I: Central Nervous System. Section II: Head and Neck. Section III. Abdomen. Section IV: Pelvis. Section V: Thorax. Second edition. Paper. Loose-leaf. Price, $2.50; $3.50; $2.25; $1.50; $1.75; $15, per set of 7 sections. 48 plates; 63 plates; 37 plates; 33 plates; 30 plates. Baltimore: William Wood & Company, 1937.

Any work on the subject of anatomy is usually useful. These handsome illustrations are no exception. Bound in loose-leaf and printed on one side of the paper, they are evidently intended for the student as a guide for his notebook and his dissection. The sections under review exclude the limbs but contain more than 200 plates on regional anatomy of the rest of the body. The drawings are diagrammatic, many in color. Usually they are replete with legend, at times seemingly cluttered. No doubt these illustrations can aid in clarifying to the student many anatomic mazes, but the various large textbooks, of the size and quality of Gray's, are cheaper and perhaps still best for the medical student, old and young.

Synopsis of Digestive Diseases. By John L. Kantor, Ph.D., M.D., Associate in Medicine, Columbia University, New York. Fabrikoid. Price, $3.50. Pp. 302, with 40 illustrations. St. Louis: C. V. Mosby Company, 1937.

This pocket size book presents a clear and concise, though necessarily abbreviated, account of the field of gastro-enterology. The book is attractively printed, the style lucid and direct. Statistical evidence is drawn from the author's large practice. The discussion on treatment is in many cases inadequate. However, classic symptomatology is well presented.

Diseases of the Soft Structures of the Teeth and Their Treatment: A Text-book for Students and Practitioners. By Hermann Prinz, A.M., D.D.S., M.D., Professor of Materia Medica and Therapeutics, the Thomas W. Evans Museum and Dental Institute School of Dentistry, University of Pennsylvania, Philadelphia. Second edition. Cloth. Price, $6.50. Pp. 500, with 308 illustrations. Philadelphia: Lea & Febiger, 1937.

This deals only with diseases of the pulp, gingivae and peridental membrane and fits the teaching program in many dental schools. This fact and the general excellence of the text account for the popularity of the first edition. The section on pulp diseases and root canal treatment is unusually complete and authoritative; the part on pyorrhea is least satisfactory. The brief historical reviews are unusually complete and enlightening. The text is replete with formulas and prescriptions where drug treatment is indicated. The disease classifications are redundant and in places confusing, as are also disease names. Dental students and dentists will find this to be a useful aid in the practice of their art.

Principles of Roentgenological Interpretation. By L. R. Sante, M.D., Professor of Radiology, St. Louis University School of Medicine, St. Louis, Missouri. Cloth. Price, $5.50. Pp. 340, with 333 illustrations. Ann Arbor, Michigan: Edwards Brothers, Inc., 1937.

This textbook is printed in typewritten letters, and all the illustrations are given only by schematic drawings; nevertheless it is an excellent book for the beginner as well as for the expert in x-rays. It is of greater value to be informed by clear drawings than by poorly reproduced pictures, since there is always a great difference between the original films and the reprints. The author classifies the whole of roentgenology in twenty-three chapters. At the end of each chapter, questions are given concerning its special content. The index is rich. Also suggestions are made for collateral reading. The textbook is one of the best we have, and it is a good supplement to the author's book on roentgenologic technic.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Right of Trial Court to Order Physical Examination of Plaintiff in Personal Injury Action.—The plaintiff sued the defendant for damages for certain injuries to her mouth, teeth and face allegedly resulting from an automobile collision which admittedly was due to the defendant's negligence. At the trial, on the direction of her attorney, she exhibited her injuries to the jury. The defendant then requested the court to require the plaintiff to submit to an examination by a dentist to be selected by the court to determine the amount of injury inflicted. This the trial court refused to do, stating that it believed that it was without authority to do so. From a judgment for the plaintiff, the defendant appealed to the Supreme Court of Oklahoma.

In this case, said the Supreme Court, the sole questions for the jury to determine were the nature and extent of the plaintiff's injuries and the amount of damages to be awarded therefor. Under these circumstances the exhibition by the plaintiff of the injured portions of her face and mouth could have had but one purpose, namely, to enhance the amount of damages to be awarded by the jury. While the courts are in disagreement as to the authority to require a plaintiff to submit to an examination in the first instance, they are in practical unanimity with respect to the rule to be followed when the plaintiff has offered a portion of his body in evidence, holding that then the plaintiff's body becomes an exhibit in the case and that within reasonable limitations the opposite party has a right to make such inspection of it as will enable him to explain, criticize or impeach its value as evidence and to that end have it examined by experts. The Supreme Court, holding that the trial court erred in not ordering the examination requested by the defendant, reversed the judgment of the trial court and ordered a new trial.—*Jewel Tea Co. v. Ransdell (Okla.), 69 P. (2d) 69.*

Workmen's Compensation Acts: Bell's Palsy a Compensable Injury.—The claimant was employed as a saleswoman by the defendant department store. While she was showing coats to a customer, a fellow employee switched on an electric fan and subjected the claimant to a sudden draft. Bell's palsy resulted and the claimant filed a claim for an award under the workmen's compensation act of New York. A disallowance of the claim by the state industrial board was affirmed by the supreme court, appellate division, and the claimant appealed to the Court of Appeals of New York.

In this case, said the court, the claimant was struck by air propelled by an electric fan. The result was "palsy which is limited to one side of the face and is acute in onset and called

Bell's." There was a consequent distortion of the parts and of the powers of expression. In the opinion of the court, the average man would say that so swift and harsh a disablement was an accidental injury when it was so strangely suffered in the ordinary day's work. It seemed to the court that analogy, too, leads to that conclusion. "Sunstroke, strictly speaking, is a disease, but the suddenness of its approach and its catastrophic nature have caused it to be classified as an accident." The order of the supreme court, appellate division, and the determination of the state industrial board denying compensation, were therefore reversed.—*Lurye v. Stern Bros. Department Store (N. Y.), 9 N. E. (2d) 828.*

Narcotics: Possession of Growing Cannabis Plant Illegal.—The appellant, Harris, was convicted of possessing unlawfully a certain narcotic drug, to wit, cannabis, and was sentenced to serve a term of three years in the state penitentiary. He appealed to the Supreme Court of Mississippi.

Two police officers of the city of Jackson, Miss., found a plant growing in Harris's back yard which they identified as cannabis. At the time the plant was discovered it was green and growing, about 7 feet high; and had seed pods or blooms on it. A Mississippi act makes it unlawful for any person to manufacture, possess, have under his or her control, sell, prescribe, administer, dispense or compound any narcotic drug except as authorized by the act. The terms "narcotic drugs" is defined to mean coca leaves, opium, cannabis, and every substance neither chemically nor physically distinguishable from them. Subsection (13) of section 2 of the act provides:

> "Cannabis" includes the following substances under whatever names they may be designated (a) the dried flowering of fruiting tops of the pistillate plant Cannabis Sativa L., from which the resin has not been extracted, (b) the resin extracted from such tops, and (c) every compound, manufacture, salt, derivative, mixture, or preparation of, such resin, or of such tops from which the resin has not been extracted.

Harris contended that the word "cannabis" as used in the act must therefore be limited to the substances as set out above, and that cannabis in any other form must be excluded. In other words, the contention was that the legislature intended only to make the possession of the "dried flowering of fruiting tops" a crime and not the possession of the green, growing plant. With this contention, however, the Supreme Court disagreed. By the use of the word "includes" in defining cannabis, the court said, the legislature clearly indicated that it did not intend to enact an entire definition. In the opinion of the court, the legislature intended to denounce as a crime the possession of cannabis in any form. The conviction of the appellant was therefore affirmed.—*Harris v. State (Miss.), 175 So. 342.*

Evidence: Admissibility of Hospital Record.—In the trial of a personal injury suit, a physician testified on behalf of the plaintiff as to the extent of her injuries and as to the treatment he had rendered. On cross examination it was shown that the physician treated the patient at a hospital. Thereupon the defendant introduced in evidence the hospital record, signed by the physician, containing certain statements inconsistent with the testimony of the physician in court. The introduction of this hospital record in evidence, said the district court of appeal, first district, division 2, California, was not error. If the physician had not testified at the trial the hospital record would have been hearsay evidence and would have been inadmissible in evidence. But since the physician did testify, the hospital record was admissible for the purpose of impeaching his testimony.—*Heiman v. Market St. Ry. Co. (Calif.), 69 P. (2d) 178.*

Hospitals: Liability for Negligence of Nurse when Acting Under Supervision of Physician.—When, said the Supreme Court of Oklahoma, a person employs a physician of his own choice and enters a hospital to receive treatment from the physician, and the hospital furnishes nurses to assist the physician under his supervision and direction, such nurses are the servants and agents of the physician while so assisting him. The hospital is not liable for their acts of negligence while acting under the supervision and direction of the physician.—*Randolph v. Oklahoma City General Hospital (Okla.), 71 P. (2d) 607.*

Society Proceedings

COMING MEETINGS

Alabama, Medical Association of the State of, Mobile, Apr. 19-21. Dr. D. L. Cannon, 519 Dexter Ave., Montgomery, Secretary.

American Association for the Study of Neoplastic Diseases, Atlanta, Ga., Apr. 14-16. Dr. Eugene R. Whitmore, 2139 Wyoming Ave. N.W., Washington, D. C., Secretary.

American Association for Thoracic Surgery, Atlanta, Ga., Apr. 4-6. Dr. Richard H. Meade Jr., 2116 Pine St., Philadelphia, Secretary.

American Association of Anatomists, Pittsburgh, Apr. 14-16. Dr. George W. Corner, 260 Crittenden Blvd., Rochester, N. Y., Secretary.

American Association of Genito-Urinary Surgeons, Atlantic City, N. J., May 2-4. Dr. Henry L. Sanford, 1621 Euclid Ave., Cleveland, Secretary.

American Association of Pathologists and Bacteriologists, Atlantic City, N. J., May 3-4. Dr. Howard T. Karsner, 2085 Adelbert Road, Cleveland, Secretary.

American Association of the History of Medicine, Atlantic City, N. J., May 2. Dr. E. J. G. Beardsley, 1919 Spruce St., Philadelphia, Secretary.

American Association on Mental Deficiency, Richmond, Va., Apr. 20-23. Dr. E. Arthur Whitney, Washington Road, Elwyn, Pa., Secretary.

American Bronchoscopic Society, Atlantic City, N. J., Apr. 30. Dr. Lyman Richards, 319 Longwood Ave., Boston, Secretary.

American College of Physicians, New York, Apr. 4-8. Mr. E. R. Loveland, 4200 Pine St., Philadelphia, Executive Secretary.

American Gastro-Enterological Association, Atlantic City, N. J., May 2-3. Dr. Russell S. Boles, 1901 Walnut St., Philadelphia, Secretary.

American Laryngological Association, Atlantic City, N. J., May 2-4. Dr. James A. Babbitt, 1912 Spruce St., Philadelphia, Secretary.

American Laryngological, Rhinological and Otological Society, Atlantic City, N. J., Apr. 27-29. Dr. C. Stewart Nash, 277 Alexander St., Rochester, N. Y., Secretary.

American Neurological Association, Atlantic City, N. J., May 2-6. Dr. Henry A. Riley, 117 East 72d St., New York, Secretary.

American Orthopedic Association, Atlantic City, N. J., May 3-5. Dr. Ralph K. Ghormley, 110 Second Ave. S.W., Rochester, Minn., Secretary.

American Society for Clinical Investigation, Atlantic City, N. J., May 2. Dr. J. M. Hayman Jr., 2065 Adelbert Road, Cleveland, Secretary.

American Surgical Association, Atlantic City, N. J., May 2-4. Dr. Charles G. Mixter, 319 Longwood Ave., Boston, Secretary.

Arizona State Medical Association, Tucson, Apr. 21-23. Dr. D. F. Harbridge, 15 East Monroe St., Phoenix, Secretary.

Arkansas Medical Society, Texarkana, Apr. 18-20. Dr. W. R. Brooksher, 602 Garrison Ave., Ft. Smith, Secretary.

Association of American Physicians, Atlantic City, N. J., May 3-5. Dr. Hugh J. Morgan, Vanderbilt University Hospital, Nashville, Tenn., Secretary.

California Medical Association, Pasadena, May 9-12. Dr. F. C. Warnshuis, 450 Sutter Street, San Francisco, Secretary.

Conference of State and Provincial Health Authorities of North America, Washington, D. C., Apr. 9-11. Dr. A. J. Chesley, Minnesota State Office Bldg., St. Paul, Secretary.

Congress of American Physicians and Surgeons, Atlantic City, N. J., May 3-4. Dr. John T. King Jr., 1210 Eutaw Place, Baltimore, Secretary.

District of Columbia, Medical Society of the, Washington, May 4-5. Dr. C. B. Conklin, 1718 M St. N.W., Washington, Secretary.

Florida Medical Association, Miami, May 9-11. Dr. Shaler Richardson, 111 W. Adams St., Jacksonville, Secretary.

Georgia, Medical Association of, Augusta, Apr. 26-29. Dr. Edgar D. Shanks, 478 Peachtree St. N.E., Atlanta, Secretary.

Hawaii Territorial Medical Association, Honolulu, May 20-22. Dr. Douglas B. Bell, Dillingham Bldg., Honolulu, Secretary.

Illinois State Medical Society, Springfield, May 17-19. Dr. Harold M. Camp, Lahl Bldg., Monmouth, Secretary.

Iowa State Medical Society, Des Moines, May 11-13. Dr. Robert L. Parker, 3510 Sixth Ave., Des Moines, Secretary.

Kansas Medical Society, Wichita, May 9-12. Mr. C. G. Munns, 112 West Sixth St., Topeka, Executive Secretary.

Louisiana State Medical Society, New Orleans, May 2-4. Dr. P. T. Talbot, 1430 Tulane Ave., New Orleans, Secretary.

Maryland, Medical and Chirurgical Faculty of, Baltimore, Apr. 26-27. Dr. Walter Dent Wise, 1211 Cathedral St., Baltimore, Secretary.

Mississippi State Medical Association, Jackson, Apr. 19-21. Dr. T. M. Dye, McWilliams Bldg., Clarksdale, Secretary.

Missouri State Medical Association, Jefferson City, May 2-4. Dr. E. J. Goodwin, 634 N. Grand Blvd., St. Louis, Secretary.

Nebraska State Medical Association, Lincoln, Apr. 26-28. Dr. R. B. Adams, Center-McKinley Bldg., Lincoln, Secretary.

New Hampshire Medical Society, Manchester, May 17-18. Dr. Carleton R. Metcalf, 5 South State St., Concord, Secretary.

New Jersey, Medical Society of, Atlantic City, May 17-19. Dr. Alfred Stahl, 55 Lincoln Park, Newark, Secretary.

New York, Medical Society of the State of, New York, May 9-12. Dr. Peter Irving, 2 East 103d St., New York, Secretary.

North Carolina, Medical Society of the State of, Pinehurst, May 2-4. Dr. T. W. M. Long, Roanoke Rapids, Secretary.

Ohio State Medical Association, Columbus, May 11-12. Mr. C. S. Nelson, 79 East State St., Columbus, Executive Secretary.

Oklahoma State Medical Association, Muskogee, May 9-11. Dr. L. S. Willour, Third and Seminole, McAlester, Secretary.

Philippine Islands Medical Association, Zamboanga City, Apr. 27-29. Dr. A. S. Fernando, 817 Taft Ave., Manila, Secretary.

Society for the Study of Asthma and Allied Conditions, Atlantic City, N. J., Apr. 30. Dr. W. C. Spain, 116 East 53d St., New York, Secretary.

South Carolina Medical Association, Myrtle Beach, May 17-19. Dr. E. A. Hines, Seneca, Secretary.

South Dakota State Medical Association, Huron, May 9-11. Dr. Clarence E. Sherwood, 102½ Egan Ave. S., Madison, Secretary.

Tennessee State Medical Association, Nashville, Apr. 12-14. Dr. H. H. Shoulders, 706 Church St., Nashville, Secretary.

Texas, State Medical Association of, Galveston, May 9-12. Dr. Holman Taylor, 1404 West El Paso St., Fort Worth, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers in continental United States and Canada for a period of three days. Periodicals are available from 1927 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them. Titles marked with an asterisk (*) are abstracted below.

American Journal of Clinical Pathology, Baltimore

8: 1-40 (Jan.) 1938

*Vaccination Against Experimental Meningococcic Meningitis. J. A. Kolmer, with assistance of Anna M. Rule, Philadelphia.—p. 1.
*Streptococcus Vaccines in Prevention and Treatment of Respiratory Infections: Clinical and Experimental Study. E. C. Rosenow and F. R. Heilman, Rochester, Minn.—p. 17.
Peripelvic Lymphatic Cysts of Kidney: Review of Literature on Perinephric Cysts. J. C. Henthorne, Rochester, Minn.—p. 28.
*Wassermann Reaction in Infectious Mononucleosis: Report of Case with Unusual Clinical Features. B. Hatz, Brooklyn.—p. 39.
Venous and Peripheral Red Blood Cell Values. Marjory I. Andresen and E. R. Mugrage, Denver.—p. 46.
Spontaneous Rupture of Myocardium. T. K. Rathmell, Norristown, Pa. —p. 52.
Histogenesis, Classification and Identification of Cells of Blood and Marrow Based on Cultures and Hematologic Studies of Human Marrow and Blood. E. E. Osgood, Portland, Ore.—p. 59.
Mechanism of Production of Acidosis. S. T. Helms, Baltimore.—p. 75.

Vaccination Against Experimental Meningococcic Meningitis.—Kolmer immunized guinea pigs, rabbits and monkeys with the subcutaneous injection of from three to five weekly doses of types I and III meningococcus vaccines cultivated in hormone broth for five days and sterilized with tricresol. All have shown the production of varying amounts of agglutinin. The serums of immunized monkeys also showed the presence of complement fixing antibody. Four weeks after the last doses of the vaccines the guinea pigs and rabbits were tested for acquired resistance by the intracisternal inoculation of living virulent meningococci. The monkeys were tested by the intraspinal inoculation of the organisms. All of twelve unvaccinated control guinea pigs died from severe meningitis in from twenty-four to seventy-two hours. Of twenty-eight vaccinated animals, five recovered. Of twelve unvaccinated control rabbits, ten died. Of twenty-eight immunized animals, fifteen died and thirteen recovered. All of six unvaccinated control monkeys showed moderately severe symptoms of meningitis but recovered. Of thirteen immunized animals, three probably showed symptoms of meningitis with recovery while the remaining ten remained entirely well. These results are believed to lend encouragement to efforts for the vaccination of human beings against meningococcic meningitis.

Streptococcus Vaccines and Respiratory Infections.—Rosenow and Heilman placed large amounts of streptococci freshly isolated from colds and influenza in a menstruum of glycerin-saline solution in the hope that suitable preventive and curative vaccines might be thus available in advance of subsequent outbreaks of epidemic respiratory infections. Through the cooperation of physicians in various parts of the United States and Canada to whom the vaccine was sent they were able to make a further study of this inherently difficult and important problem. The persons vaccinated were chiefly those who were abnormally susceptible to recurring respiratory infections. In the great majority of the different groups representative of different climatic conditions, the incidence of colds and of influenza was greatly reduced. A lesser number were slightly benefited and few were not benefited. There were eleven separate camps of the CCC in Minnesota, in each of which some of the men were vaccinated and some were not. In three other camps all men had been vaccinated, and in ten additional camps, also in Minnesota, none were vaccinated. The incidence of colds or influenza was consistently from a third to a half as great among the vaccinated as among the unvaccinated. In each of the fourteen subgroups of which some were and some were not vaccinated, the vaccinated subjects fared better as regards incidence, severity and duration of respiratory infections than did the unvaccinated controls.

Wassermann Reaction in Infectious Mononucleosis.—Hatz, in treating a case of infectious mononucleosis, investigated the connection between a positive Wassermann test and a positive heterophile sheep cell agglutination test. Clinically the case was of interest because the complete absence of enlargement of lymph nodes or spleen, coupled with the age of the patient (41 years), could readily have led to a diagnosis of "influenza" or "grip" if proper blood studies had not been made. Serologically, a positive Paul-Bunnell test and a positive Wassermann associated with a negative Kline test were obtained. As the patient recovered, both the Paul-Bunnell and Wassermann tests became negative. This seems to point to a similarity in the mode of formation of the antibodies concerned.

American J. Obstetrics and Gynecology, St. Louis

35: 1-188 (Jan.) 1938

Low Reserve Kidney. H. J. Stander and K. Kuder, New York.—p. 1.
*Leukoplakia, Leukokeratosis and Carcinoma of Cervix. W. Schiller, New York.—p. 17.
Theca Cell Tumors. S. H. Geist and J. A. Gaines, New York.—p. 39.
Disease of Spinal Cord in Pregnancy: Myelopathy of Pregnancy: Clinicopathologic Study. W. Needles and C. Davison, New York.—p. 52.
Functional Uterine Bleeding, with Especial Reference to That Associated with Secretory Endometrium. H. W. Jones, Baltimore.—p. 64.
Biology of Human Vagina in Pregnancy. M. E. Davis and S. A. Pearl, Chicago.—p. 77.
*Identification of Yeastlike Organisms Isolated from Vaginal Tracts of Pregnant and Nonpregnant Women. C. P. Jones and D. S. Martin, Durham, N. C.—p. 98.
Blood Picture of Pregnancy. H. G. Watson, San Francisco.—p. 106.
*Quantitative Determination of Estrogenic Substances in Normal Female Urine During Menstrual Cycle. R. G. Gustavson, L. W. Mason, E. E. Hays, T. R. Wood and F. E. D'Amour, Denver.—p. 115.
Study of 285 Cases of Breech Delivery. W. C. Danforth and C. E. Galloway, Evanston, Ill.—p. 123.
Prolongation of Pregnancy in Rabbit by Injection of Progesterone. G. P. Heckel and W. M. Allen, Rochester, N. Y.—p. 131.
Quinine Iodobismuthate in Treatment of Syphilis Complicating Pregnancy. M. A. Castallo and A. E. Rakoff, Philadelphia.—p. 137.
Short Wave Therapy in Gynecology and Obstetrics: Experiences with 120 Cases. E. G. Waters, Jersey City, N. J.—p. 143.
Postpartum Hypertension Following a Normal Pregnancy. H. Meyer, New Orleans.—p. 150.
Basal Metabolic Rate in Normal Pregnancy. G. C. Hanna Jr., Philadelphia.—p. 155.
Superimposed Lipemia During Labor. E. M. Boyd and G. Mylks Jr., Kingston, Ont.—p. 160.
Myxedema with Menorrhagia and Tetany as Complications Following Partial Thyroidectomy. C. W. Dunn and W. R. Nicholson, Philadelphia.—p. 165.
Lateral Vaginal Wall Retractor. M. C. Piper, Rochester, Minn.—p. 169.

Leukoplakia and Carcinoma of Cervix.—According to Schiller, the relationship between leukoplakia and carcinoma is confused by the question as to whether the leukoplakia is not merely a precarcinomatous stage of the portio. The entire situation is thrown into further confusion by the improper use of the word "precancerous" or "precarcinomatous." The use of the word in diagnosis should be discarded, its use being restricted to symptomatic description. The diagnosis of the disorder that appears as leukoplakia should be made only on microscopic observation. The differences between the forms of leukoplakia can frequently be recognized with the naked eye or by a colposcopic examination. However, patches which differ slightly in color from the surrounding normal tissue may be overlooked during a hasty examination. In such cases iodine is useful. The application of iodine makes the grossly visible leukoplakia appear clearer and the latent leukoplakia visible to the naked eye. If there is a beginning carcinoma in the latent leukoplakia, the iodine will reveal its presence even if other clinical methods fail. Cornification and carcinoma give rise to manifest or latent patches. This observation proves that there are leukoplakias which are definitely carcinomas, or at least carcinoid or carcinomatous epithelium. Leukoplakias which show definite carcinomatous changes and fulfil all of Schottlander's and Kermauner's criteria for carcinomatous "beläge" are admitted as "potential" carcinomas, even by observers who are diagnosing carcinoma by invasion only. If in addition there is an invasive growth, even the most critical observer will be convinced that it is malignant. The only fact of importance is that the superficial carcinoma-

tous layer, which sometimes resembles a leukoplakia, may retain its superficial character for months or years before becoming invasive. The answer to the question whether such leukoplakias can become malignant is that they are already malignant. Leukoplakias formed through cornification should be differentiated in terminology. This can be done easily by borrowing a term from laryngology, in which similar changes are called leukokeratosis. Cornification may be incomplete or complete. The former is called parakeratosis and the latter keratosis. Excessive hornification is termed hyperkeratosis. Leukohyperkeratosis is a higher degree of leukokeratosis. A certain degree of cutaneous cornification is physiologic. However, a hyperkeratosis is pathologic. Leukokeratosis is used to denote cornification in general. The author has only once found areas of leukoparakeratosis or leukohyperkeratosis developing into carcinoma. There is no causal relationship between parakeratosis or hyperkeratosis and carcinoma of the portio. Advanced cornification, even the autonomous form, does not give rise to carcinoma. Areas of leukoplakia do not warrant radical treatment. A periodic examination is sufficient. These areas of leukoplakia are to be grouped with benign hyperkeratosis of the skin rather than with the leukoplakic areas of the mucosa of the mouth or larynx. A suggestive area of the portio when examined microscopically will turn out to be either a leukokeratosis or a carcinomatous layer ("belag"). The difference between the two is so marked that there is never a question of differential diagnosis. Proliferations of the epithelium, however, due to chronic inflammation do cause confusion sometimes.

Yeastlike Organisms Isolated from Vaginal Tracts.—Jones and Martin isolated sixty-eight strains of yeastlike fungi from the vaginas of fifty-two pregnant and sixteen nonpregnant women. These strains have been identified and compared with type species of Benham and Stovall by developing a technic that can be carried out in a routine bacteriologic laboratory and that does not require special mycologic training.

Estrogenic Substances During Menstrual Cycle.—Gustavson and his associates present the graphs of three women, all entirely normal from gynecologic and general points of view. Since a particular ovulation and developing corpus luteum are the controlling factors in the next subsequent menstruation, the relation that the peaks in the graphs bear to the time of the next menstrual period in each case were observed. Neither of the two peaks bears any constant relation to the time of the next menstruation, nor do they to each other. This variation is seen in the graphs of different individuals and in different cycles in the same individual. One of two conclusions is indicated: (1) Either the time of ovulation may vary considerably from cycle to cycle in the same individual, and be considerably different in different individuals, and the corpus luteum may require varying periods of time to reach its full development and activity or (2) the peaks of estrogenic excretion, presuming peaks of concentration in the blood, have no particular relationship to ovulation and corpus luteum activity. With the constancy with which these two peaks appear in the graphs obtained from daily twenty-four hour specimens in normal individuals, the first conclusion seems to be more logical.

American Journal of Ophthalmology, St. Louis

21: 121-238 (Feb.) 1938

Benzedrine in Cycloplegia: II. Further Report. S. J. Beach and W. R. McAdams, Portland, Maine.—p. 121.
Optical Decentration of the Eye. A. I. Dashevsky and D. G. Booshmitch, Kharkof 23 (Ookrinah) U. S. S. R.—p. 125.
Neuromyelitis Optica: Report of Two Cases. S. H. McKee and F. L. McNaughton, Montreal.—p. 130.
Chronic Cellular Infiltration of Uvea in Septic Endophthalmitis of Ectogenous Origin. H. D. Lamb, St. Louis.—p. 137.
Diagnosis and Treatment of Phorias. W. T. Davis, Washington, D. C.—p. 145.
Measurement of Angle of Maximal Convergence. H. G. Martin, Milwaukee.—p. 161.
Occurrence of So-Called Dinitrophenol Cataracts Without Ingestion of Dinitrophenol. H. Barkan and J. W. Bettman, San Francisco.—p. 165.
Analysis of Seventy-One Consecutive Cases of Unilateral Exophthalmos. M. E. Randolph, Baltimore.—p. 169.
Treatment of Ocular Syphilis. D. Kravitz, Brooklyn.—p. 176.
Muscle Weakening by Central Tenotomy. W. G. Watrous and J. M. D. Olmsted, Berkeley, Calif.—p. 182.

American Journal of Orthopsychiatry, Menasha, Wis.

8: 1-184 (Jan.) 1938

Conditioned Reflex and Psychiatry of Infancy. A. Gesell, New Haven, Conn.—p. 19.
Stanford-Binet Response Patterns in Epileptics. A. Louise Collins, C. R. Atwell and M. Moore, Boston.—p. 51.
Relationship Therapy. J. Levy, New York.—p. 64.
Criminally Aggressive Behavior in Passive, Effeminate Boys. Martha Wilson Macdonald, Chicago.—p. 70.
Psychometric Practice in Adults of Superior Intelligence (III). F. L. Wells, Boston.—p. 79.
The Graphic Arts. E. Liss, New York.—p. 95.
Scoring the Rorschach Test with Specific Reference to "Normal Detail" Category. Marguerite R. Hertz, Cleveland.—p. 100.
Role of Parents in Development of Emotional Instability. R. Stagner, Akron, Ohio.—p. 122.
*Psychiatric Study of Car Sickness in Children. J. H. Conn, Baltimore.—p. 130.
The Meaning of Time for Children. W. Bromberg, New York.—p. 142.
Role of Institution in Treatment of Delinquency. Grace Grossmann, Brooklyn.—p. 148.
Instance of Social Origin of Conflict Resulting in Psychoses. J. M. Hunt, Providence, R. I.—p. 158.

Psychiatric Study of Car Sickness.—Conn compared twenty-five car-sick children (thirteen girls and twelve boys) between 6 and 12 years of age with a group of twenty-five patients who were not car sick. The personality of the child and his life situation appeared significant in the occurrence of car sickness. All of the twenty-five car-sick children were described as being emotionally unstable; seventeen were timid and submissive in make-up. Among the complaints associated with the car sickness were restlessness, difficulty in falling asleep, nail biting, fear of the dark, enuresis and episodes of vomiting. Nineteen of the patients were found to be poorly nourished. Six children were of superior intelligence, five were of limited intelligence and fourteen were of average intelligence. The influence of the life situation was illustrated by a series of play contacts. In several cases the fears of the dark, general apprehensiveness and timidity improved in association with the disappearance of the car sickness. One child vomited while riding in a street car and in an automobile but was not disturbed while riding in a taxicab. Another patient was car sick only during the winter months. When the child was given a chance to express himself about his experiences on the street car and automobile, it was possible to begin to understand such reactions. In the verbatim reports of the play reactions there was no instance in which a car-sick child stated that the doll was at ease in the toy street car. Nor did a child who was not car sick report the anticipation of an accident or speak of the fearfulness of the doll in the toy street car.

American Journal of Pathology, Boston

14: 1-124 (Jan.) 1938

Role of Cells of Schwann in Formation of Tumors of Peripheral Nerves. P. Bailey and J. D. Herrmann, Chicago.—p. 1.
Pathology of Granuloma Venereum. R. D'Aunoy and E. von Haam, New Orleans.—p. 39.
Pneumoconiosis and Pulmonary Carcinoma. A. J. Vorwald and J. W. Karr, Saranac Lake, N. Y.—p. 49.
*Tuberculous Meningitis and Its Relation to Tuberculous Foci in the Brain. D. Beres and T. Meltzer, New York.—p. 59.
Experimental Study of Complement and Hemolytic Amboceptor Introduced into Chick Embryos. Alice Polk, G. J. Buddingh and E. W. Goodpasture, Nashville, Tenn.—p. 71.
Failure of Allergic Inflammation to Protect Rabbits Against Infection with Virulent Pneumococci. P. R. Cannon and G. Hartley Jr., Chicago.—p. 87.
Fatty Infiltration and Cirrhosis of Liver in Depancreatized Dogs Maintained with Insulin. I. L. Chaikoff, Berkeley, Calif.; C. L. Connor and G. R. Biskind, San Francisco.—p. 101.
Pathologic Changes in Placenta Associated with Erythroblastosis of Fetus. L. M. Hellman and A. T. Hertig, Boston.—p. 111.
Calcification of Aorta, Heart and Kidneys of Albino Rat. Katharine Pattee Hummel and L. L. Barnes, Ithaca, N. Y.—p. 121.

Tuberculous Meningitis and Tuberculous Foci in the Brain.—Beres and Meltzer made an anatomic survey of twenty-eight cases of tuberculous meningo-encephalitis and of two cases of tuberculoma without meningitis. In all cases of tuberculous meningitis there was an extension of the inflammatory process into the cortex resulting in foci of encephalitis, which varied in degree from perivascular infiltration to tubercle formation. In a few cases solitary tubercles were found, but these were not in contact with the ependyma or leptomeninges. When tubercles

occurred in great numbers, they were due to direct hematogenous dissemination. Large solitary tuberculomas occurred with or without meningitis. Cortical tubercles which might have been responsible for the coexistent meningitis were demonstrated in only six cases. In eleven cases the choroid plexus disclosed the presence of tubercle formation. The changes in the blood vessels which were observed during the course of the study presented no observations that differed from those already described by other authors.

Annals of Internal Medicine, Lancaster, Pa.

11: 1077-1394 (Jan.) 1938

*Treatment of Rheumatoid Arthritis with an Injectable Form of Bee Venom. J. Kroner, R. M. Lintz, Marian Tyndall, Leonora Andersen and Edith E. Nicholls, New York.—p. 1077.
Mechanism of Toxic Effects from Combined Use of Calcium and Digitalis. J. S. Golden and W. A. Brams, Chicago.—p. 1084.
The Present Status of Rheumatism and Arthritis: Review of American and English Literature for 1936 (Fourth Rheumatism Review). P. S. Hench, Rochester, Minn.; W. Bauer, Boston; D. Ghrist, Los Angeles; F. Hall, Boston; W. P. Holbrook, Tucson, Ariz.; J. A. Key, St. Louis, and C. H. Slocumb, Rochester, Minn.—p. 1089.
Rare Manifestation of Gout: Widespread Ankylosis Simulating Rheumatoid Arthritis. A. O. Ludwig, G. A. Bennett and W. Bauer, Boston.—p. 1248.
*Uric Acid in Serum of Gouty and Nongouty Individuals: Its Determination by Folin's Recent Method and Its Significance in Diagnosis of Gout. B. M. Jacobson, Boston.—p. 1277.
"Platelike" Atelectasis of Lung. Alice Ettinger, Boston.—p. 1296.
Comparison of Pressures in Arm Veins and Femoral Veins, with Especial Reference to Changes During Pregnancy. C. S. Burwell, Boston.—p. 1305.
*Splenic Irradiation in Treatment of Purpura Haemorrhagica. H. W. Jones, L. M. Tocantins and R. M. Smith, Philadelphia.—p. 1311.
Effects of Insulin Hypoglycemia on Diabetic Heart in Children and Youth. H. F. Root, Boston.—p. 1332.
Unilateral Hemoglobinuria: Its Occurrence in Infarction of Kidney. E. Libman and A. M. Fishberg, New York.—p. 1344.
Present Mortality of Diabetic Children: Remediable and Therefore Hopeful Index of the Future of the Diabetic Child. E. P. Joslin, Boston.—p. 1348.

Rheumatoid Arthritis Treated with Bee Venom.—Kroner and his colleagues gave intradermal injections of bee venom (apicosan) to 100 patients with rheumatoid arthritis; seventy-three of these showed definite improvement, as judged by a fall in the corrected sedimentation index and an alleviation of the clinical symptoms. Seventeen were found to be entirely free from symptoms six months to a year after the treatments were discontinued, eighteen continued to have only mild transitory pains and thirty-eight were moderately improved. Ten of the patients studied had an advanced, active deforming type of arthritis and six of these showed moderate improvement. A patient was not considered improved unless there was a drop in the corrected sedimentation index, if previously elevated, as well as improvement in the clinical symptoms. Of the ten patients with advanced arthritis the number of injections for the six who improved was from eight to fifty-two, with an average of 31.5, while the four who failed to improve had from nine to twenty-eight, with an average of 18.5 injections. The duration of treatment for the former varied from two to fourteen months, and for the latter from two to four months. For the patients with a moderately severe arthritis the range of injections was from six to forty-eight and for the patients with a mild arthritis from six to thirty-eight. All injections were given intradermally. The site selected depended on the location of the most painful joints. The skin was cleansed with alcohol and wiped dry with benzene. The treatments were continued at weekly or biweekly intervals, increasing 0.1 cc. at each visit. Only 0.1 cc. was put into a wheal and the wheals were placed about 1 inch (2.5 cm.) apart. When a patient had received 0.5 cc. of concentration I, he was given 0.1 cc. of concentration II, which was increased to 0.5 cc., and then concentration III was started. The dose was then increased 0.1 cc. at each visit until the patient was receiving one ampule of concentration III. All injections were watched for five minutes. If large pseudopodia developed in the wheals, they denoted sensitivity and the dose was not increased for several visits.

Uric Acid in Gouty and Nongouty Individuals.—Jacobson employed the recent Folin method in the study of the uric acid in the serum of gouty and nongouty individuals. The analysis of serum derived from blood allowed to clot under oil furnishes more valid data than does whole blood. The fasting uric acid in 100 nongouty persons consuming a mixed diet ranged from 1.9 to 6.7 mg. per cent. In ninety-seven persons the uric acid in the serum was less than 6 mg. per hundred cubic centimeters; it was determined on 177 occasions in twenty-one cases of gout, under various conditions. Its values ranged from 5.2 to 14.8 mg. per hundred cubic centimeters. On 174 occasions the value exceeded 6 mg. and on 167 occasions 7 mg. The consumption by gouty individuals of a purine-free diet during periods shorter than three months did not significantly influence the level of uric acid in the serum. The administration of acetylsalicylic acid, colchicine and salyrgan to gouty persons on several occasions was followed by an apparent temporary fall of the uric acid level. The uric acid in the serum, frequently determined in four gouty persons, exhibited marked fluctuation both during asymptomatic intervals and during attacks of acute gouty arthritis. An intensive study of one case over a period of one year demonstrated a significant fall of the mean uric acid level during a period of three days preceding attacks of acute gouty arthritis; during the attacks the level of uric acid in the serum remained unchanged. In four cases of gout there was an apparent direct correlation between the height of the level of uric acid in the serum and the severity of the disease.

Splenic Irradiation in Hemorrhagic Purpura.—In twelve patients with hemorrhagic purpura who received irradiation to the spleen, Jones and his associates found the response to roentgen therapy ineffective. An increase in platelets occurred in one patient but did not persist after further roentgen treatment. Many of the patients received 200 roentgens without favorable response. It seems probable that there are certain patients with this disease who will respond in a manner such as described by Mettier and others, and that there are other patients with the same disease who will fail to respond to adequate roentgen treatment. The authors' plan of treatment is as follows: If the patient is not in a dangerous state from loss of blood, they give him an opportunity to recover without any special form of treatment. If there is progressive anemia, small transfusions are used. These are given every two or three days or at times more often or in larger doses. Vitamin C is given intravenously in selected cases. Liver extract is given intramuscularly and orally. The use of snake venom and x-rays in sufficient doses is continued in all patients in whom it is safe, and finally, when all other measures fail, splenectomy is resorted to. In one patient who had an acute intra-abdominal condition there was a sudden drop in red blood cells following roentgen therapy and in a patient with a long bleeding time intracranial hemorrhage developed and the patient died after roentgen treatment, probably as a result of retching and vomiting.

Archives of Pathology, Chicago

25: 149-302 (Feb.) 1938

*Mechanism of Shock: Effects of Intravenous Injection of Salt Solution in Collapse Induced by Mechanical Impounding of Blood in Splanchnic Region in Normal and in Hyperthyroid Dogs. Opal E. Hepler and J. P. Simonds, Chicago.—p. 149.
Spontaneous and Experimental Amebic Infection in Reptiles. H. L. Ratcliffe, Philadelphia, and Q. M. Geiman, Boston.—p. 160.
Multiple Mesenchymal Hemendothelioma: Report of Case. S. M. Rabson, New York.—p. 185.
Reaction of Lymphatic Tissue in Early Stages of Bacterium Monocytogenes Infection. Eleanor A. Conway, Chicago.—p. 200.
Evidences of Syphilis in Mound Builders' Bones: Gross Pathologic Study. W. L. Haltom, Martinsburg, W. Va., and A. R. Shands Jr., Wilmington, Del.—p. 228.
Recent Contributions to Immunology of Helminthic Infections. J. T. Culbertson, New York.—p. 256.

Mechanism of Shock.—Hepler and Simonds find that, when blood is impounded in the liver and gastro-intestinal tract by mechanical constriction of the hepatic veins in dogs, the systemic blood pressure falls abruptly to a level equivalent to from 35 to 70 per cent of the original pressure and is maintained for periods of at least thirty minutes. Injection of physiologic solution of sodium chloride during constriction of the hepatic veins in quantities more than the estimated initial blood volume induces a rise in systemic blood pressure during the injection, but the pressure falls almost to the previous low level within one to three minutes after the injection is stopped. The blood volume after injection of the solution and while the

hepatic veins are still constricted may be either greater or less than the calculated initial volume and the saline solution injected. Blood volumes after release of the hepatic veins were invariably much lower than the calculated initial volumes and the saline solution injected. The rate of fall in blood pressure and reduction in blood volume after injection of saline solution indicate the rapidity with which fluid escapes from the circulating blood when a considerable part of the total volume of blood is impounded in a known region of the body. Thyrotoxicosis in dogs adds a complicating factor in experiments of this type. In dogs submitted to injection of large amounts of saline solution much fluid was found to have escaped into the lumen of the stomach and into the gastric submucosa. The peritoneal cavity contained relatively little fluid, and the retroperitoneal tissues and the walls of the gallbladder and small intestine were moderately edematous.

Canadian Public Health Journal, Toronto

29: 1-52 (Jan.) 1938

Atmospheric Pollution in Toronto, Canada. H. M. Barrett, Toronto. —p. 1.

Adequate School Examination. G. Binning, Saskatoon, Sask.—p. 13.

Industrial Cadmium Poisoning: Report of Fifteen Cases, Including Two Deaths. F. M. R. Bulmer, H. E. Rothwell and E. R. Frankish, Toronto.—p. 19.

Isolation of Virus from Cases of Influenza in Toronto. R. Hare and Chun Hui Yen, Toronto.—p. 27.

Florida Medical Association Journal, Jacksonville

24: 363-418 (Jan.) 1938

Impaired Hearing from Certain Drugs and Chemical Poisons. H. M. Taylor, Jacksonville.—p. 377.

Traumatic Surgery. L. J. Netto, West Palm Beach.—p. 385.

Urinary Infestations with Trichomonas Vaginalis in the Male. P. D. Melvin, Miami.—p. 391.

Elliott Treatment in Thirty-Three Cases. H. Weems, Sebring.—p. 393.

Ocular Complications Following Dengue Epidemic of 1934. M. Faver, Miami.—p. 395.

Journal of Allergy, St. Louis

9: 105-210 (Jan.) 1938

Variations in Specificity of Skin-Sensitizing Antibodies in Allergy of Man, as Shown by Neutralization with Antigens. W. B. Sherman and A. Stull, New York.—p. 105.

Studies in Experimental Hypersensitiveness in Rhesus Monkey: V. Technic for Demonstrating Absorption of Undigested Protein. H. W. Straus and M. Walzer, Brooklyn.—p. 121.

*Scarlet Fever Immunization by Intracutaneous Injection of Scarlatinal Streptococcus Toxin. R. A. Kern, Jean Crump, R. L. Roddy and S. Borow, Philadelphia.—p. 125.

Acquired Specific Hypersensitivity to Simple Chemicals: I. Eczematous Sensitivity to Clothing and to Cosmetics, with Especial Reference to Dyes. J. Goodman, Boston, and M. B. Sulzberger, New York.—p. 136.

Observations on Treatment of Asthma and Related Conditions with Suprarenal Cortical Extract (Cortin). L. E. Prickman and G. A. Koelsche, Rochester, Minn.—p. 158.

Mistakes in Allergic Diagnosis and Treatment. G. L. Lambright, Cleveland.—p. 166.

Allergenic Molds in the Pacific Northwest. P. Schonwald, Seattle.—p. 175.

Gold Curve Obtained with Allergic Blood Serum. J. M. Anderson, Salt Lake City.—p. 180.

Immunization with Scarlatinal Streptococcus Toxin.—Kern and his associates report their observations during the past two years on the intracutaneous injection of scarlatinal streptococcus toxin for the production of active immunity against scarlet fever. Their test subjects included 140 children from 16 months to 13 years of age, all of whom had been found to have a positive Dick test. Twenty-six of the children were frankly allergic. Scarlatinal streptococcus toxin, as prepared by a commercial house under license by the Dick scarlet fever commission, was used. The material was that usually employed in subcutaneous injection, containing 500, 2,000, 8,000, 25,000 and from 80,000 to 100,000 skin test doses, respectively, per cubic centimeter. Each child was given weekly intracutaneous injections of toxin into the skin of the outer aspect of the upper arm. It was found that the intracutaneous injection of scarlatinal streptococcus toxin in about one-tenth the dosage employed subcutaneously will result in a negative Dick test in more than 90 per cent of susceptible subjects. Since the immunity so conferred would appear not to be as lasting as that by the full subcutaneous dosage, those immunized by the intracutaneous method should be retested every six months and, if found Dick positive, should again receive a course of injections. The intracutaneous method has the great advantage of unusual freedom from severe general reactions.

Journal of General Physiology, New York

21: 269-410 (Jan.) 1938. Partial Index

Area and Visual Threshold. G. Wald, New York and Cambridge, Mass. —p. 269.

Studies on Enzymatic Histochemistry: XXV. Micro Method for Determination of Choline Esterase and Activity Hydrogen Ion Concentration Relationship of This Enzyme. D. Glick, Copenhagen, Denmark. —p. 289.

Id.: XXVI. Histologic Distribution of Choline Esterase in Gastric Mucosa Normally and After Administration of Certain Drugs. D. Glick, Copenhagen, Denmark.—p. 297.

Concentration and Purification of Bacteriophage. J. H. Northrop, Princeton, N. J.—p. 335.

Ultracentrifugal Analysis of Concentrated Staphylococcus Bacteriophage Preparations. R. W. G. Wyckoff, Princeton, N. J.—p. 367.

Journal of Infectious Diseases, Chicago

62: 1-128 (Jan.-Feb.) 1938

Simultaneous Cutaneous and Lymphnodal Shwartzman Phenomenon. E. E. Ecker, H. T. Karsner and L. Meschan, Cleveland.—p. 1.

*Measles Inclusion Bodies in Blood and in Tissue Cultures. Jean Broadhurst, Gladys Cameron and V. Saurino, New York.—p. 6.

Tissue Cultures of Human Throat Inclusion Bodies. Jean Broadhurst, Gladys Cameron and Inez Taylor, New York.—p. 21.

Studies on Vaccinia Virus: Determination of Correlative Factors Between the Rate of Multiplication of Virus in Skin and Histologic Changes Produced. D. Widelock, New York.—p. 27.

Mucoid Phase in Dissociation of the Gonococcus. P. J. Almaden, Little Rock, Ark.—p. 36.

*Hemolytic Streptococci from Throat of Normal Young Adults. A. W. Frisch, Madison, Wis.—p. 40.

Toxicity of Young Cells of Salmonella Paratyphi A and B When Lysed by Bacteriophage. Ruth E. Gordon and C. N. Stark, Ithaca, N. Y. —p. 45.

Rate of Disappearance of Crystalline Egg Albumin Following Its Intravenous Injection. H. B. Kenton, Chicago.—p. 48.

Studies on Minute Hemolytic Streptococci: IV. Further Observations on Distribution of Ordinary and Minute Beta Hemolytic Streptococci in Normal and Diseased Human Beings. P. H. Long and Eleanor A. Bliss, Baltimore.—p. 52.

Study of Actinomyces Necrophorus in Soil Cultures. E. A. Tunnicliff, Bozeman, Mont.—p. 58.

Susceptibility of Mice to Inhaled Type III Pneumococci. E. G. Stillman, New York.—p. 66.

Chemical Composition and Antigenic Properties of Fractions of Smooth and Rough Strains of Staphylococcus Aureus. Rachel E. Hoffstadt, Seattle, and W. M. Clark, Tacoma, Wash.—p. 70.

Local Immunity to Scarlet Fever Toxin. G. F. Dick and Gladys H. Dick, Chicago.—p. 83.

*Alpha Type Streptococci in Food Poisoning. W. E. Cary, G. M. Dack and Ellen Davison, Chicago.—p. 88.

Reactions to "Tuberculin" from Unusual Type of Acidfast Bacillus: Results in 525 Children of Simultaneous Intradermal Injection of Old Tuberculin and "Tuberculin" Prepared from an Atypical Mycobacterium. P. W. Beaven, Rochester, N. Y.—p. 92.

Effects of Splenectomy and Blockade on Passive Transfer of Antibodies Against Trypanosoma Lewisi. W. H. Taliaferro, Chicago.—p. 98.

Cultural Studies on "Donovan Bodies" of Granuloma Inguinale. R. B. Dienst, R. B. Greenblatt and E. S. Sanderson, Augusta, Ga.—p. 112.

Taxonomic Relationships of Lactobacillus Bifidus (Bacillus Bifidus Tissier) and Bacteroides Bifidus. J. E. Weiss and L. F. Rettger, New Haven, Conn.—p. 115.

Relation of Anticlotting Property of Streptococcus Viridans to Dissociation and Hydrogen Ion Concentration. Ruth Tunnicliff and Carolyn Hammond, Chicago.—p. 121.

Satellite Hemolytic Zones in Blood Agar Staphylococcus Cultures. G. Bernice Rhodes, Chicago.—p. 124.

Measles Inclusion Bodies.—Broadhurst and her co-workers observed various morphologic types of inclusion bodies in measles blood taken from one day before the beginning of the rash to ten days after its appearance. These inclusion bodies are more satisfactorily demonstrated in blood smears by minimal staining with simple stains than with the customary complex blood stains. In blood smears inclusion bodies are readily demonstrable in the mononucleated types of white corpuscles. The inclusion bodies in measles blood smears include minute pinpoint bodies, somewhat larger globular bodies and compact densely staining masses, sometimes definitely crescentic. While all types of white corpuscles may show shattered cells and disintegration changes, the mononucleated corpuscles show other distinctive characters: (1) the nucleus is paler than granule-loaded cytoplasm when stained with methylene blue, (2) the

margins are bubbly or eruptive and (3) occasional bizarre extensions or protusions are seen. Many of the tissue culture cells containing inclusion bodies are highly vacuolated and are often swollen and distorted in outline, showing both "ballooning disintegration" and "colliquation."

Hemolytic Streptococci from Normal Throats.—Frisch found an incidence of forty (6.4 per cent) of group A streptococci in the throats of 621 normal adults of college age. Of 101 strains of hemolytic streptococci sixty-seven, or 66.5 per cent, lysed human fibrin, but only forty, or 39.6 per cent, were members of group A. Persons with intact tonsils harbored group A streptococci somewhat more frequently than persons whose tonsils had been removed.

Alpha Type Streptococci in Food Poisoning.—Cary and his collaborators report a large institutional outbreak of food poisoning in which streptococci were present in enormous numbers in the incriminated beef croquettes. Filtrates and living cultures were fed to seven volunteers. Another green streptococcus isolated from coconut custard pie implicated in another outbreak was similarly fed. Diarrhea was the most prominent symptom and occurred among 117 out of 208 young men. Their experience with human volunteers has indicated that living cultures of alpha type streptococci, and not filtrates, are necessary to give rise to symptoms of food poisoning in man. The incubation period corresponds to that in Salmonella type food poisoning (twelve hours), which is caused by living organisms, rather than the staphylococcic type (three hours), due to soluble enterotoxic substance.

Journal of Pediatrics, St. Louis

12: 1-138 (Jan.) 1938

Normal Gastric Secretion of Infants and Small Children Following Stimulation with Histamine. R. D. Cutter, San Francisco.—p. 1.
*Blood Coagulation Factors in Hemorrhagic Disease of the New-Born and Value of Intramuscular Injections of Father's and Mother's Blood. H. N. Sanford and Eleanor I. Leslie, Chicago.—p. 16.
Metabolism Studies on Age Disposition to Ketosis in Human Beings. W. Heymann, Cleveland.—p. 21.
*Can Sensitization Be Induced by Intracutaneous Injection of Tuberculin? W. E. Nelson, A. G. Mitchell and Estelle W. Brown, Cincinnati.—p. 26.
Prophylaxis of Poison Ivy: Use of Almond Oil Extract in Children. L. C. Bachmann, East Providence, R. I.—p. 31.
Tidal Drainage in Treatment of Acute Uncomplicated Empyema in Children. A. Weller, Boston.—p. 38.
Use of Intubation and Tracheotomy in Treatment of Obstructive Laryngitis in Children. W. A. Howard, Washington, D. C.—p. 47.
Ectopia Cordis cum Sterni Fissura: Case Study. R. N. Barlow, St. Louis.—p. 58.
Banana Therapy in Diarrheal Diseases of Infants and Children. C. L. Joslin, J. E. Bradley and T. A. Christensen, Baltimore.—p. 66.
Psychologic Care During Infancy. Ruth Morris Bakwin and H. Bakwin, New York.—p. 71.
Rheumatic Nodules. H. I. G. Anderson, Durham, N. C.—p. 91.
*Herpetic Stomatitis. Katharine Dodd, L. M. Johnston and G. J. Buddingh, Nashville, Tenn.—p. 95.

Blood Coagulation Factors in Hemorrhagic Disease.—In two infants with hemorrhagic disease of the new-born, Sanford and Leslie found the faulty coagulation to be due to a failure of the platelets to disintegrate. This is a qualitative platelet dysfunction and is an exaggeration of the platelet action in blood of the normal new-born infant. There was no evidence that small intramuscular injections of blood from the parents had any effect on the coagulation time of the blood of twenty normal new-born infants. One of the infants with hemorrhagic disease recovered after a small injection of the father's whole blood intramuscularly. The second infant recovered without treatment of any kind.

Tuberculin Sensitization by Intracutaneous Injection.—Nelson and his colleagues tried to determine whether tuberculin in amounts as great as or slightly greater than ordinarily used for skin testing is capable of inducing sensitization to itself in man. If this were the case, tuberculin testing after the initial injection would be valueless for the detection of tuberculous infection. Their evidence does not support the theory of artificially induced tuberculin sensitization by single or repeated intracutaneous tuberculin injections for the following reasons: 1. The third injection was performed ninety-six hours after the first test, an interval presumably too short to permit induction of sensitization. 2. A consistent individual response was not obtained. 3. Neither were consistent maximal rates or sizes of reactions obtained in later tests. 4. X-ray evidence, usually accepted as diagnostic of tuberculous lesions, in children of all groups who had no or only questionably positive reactions in the first two tests indicated that tuberculous lesions may be associated with a low degree of tuberculous allergy. This does not imply that sensitization to tuberculin or tuberculoprotein is impossible, but such sensitization does not appear likely from the ordinary use of tuberculin for purposes of cutaneous testing.

Herpetic Stomatitis.—In the last eleven years Dodd and her associates have seen in the Vanderbilt Hospital Children's Clinic eighty-eight cases of a form of stomatitis which appears to be a clinical entity. The disease occurred in children from a few weeks to 14 years of age but was far more common in children between the ages of 1 and 3 years. The disease was apparently contagious, as sometimes two cases were seen in the same family or there was a history that the patient had recently been in contact with a child having a similar condition. The stomatitis was apparently identical with that described in most pediatric textbooks as aphthous stomatitis. There appears to be a sudden onset of illness with fever, general malaise and loss of appetite. Either with the onset of fever, or twenty-four hours or more later, lesions appear in the mouth. When these were seen early, they consisted of reddish blisters of the mucous membrane. Soon the blisters became ulcerated and the ulcers were covered by a yellowish white membrane. The commonest sites of the lesions were the tongue, the inner surface of the lips and the buccal and sublingual mucous membrane. In every instance there were, besides the local lesions, marked redness and swelling of the gums with a tendency to bleed easily. Salivation was greatly increased. The older children complained of soreness of the mouth and pain on eating; the younger ones were irritable and often refused to eat or drink anything. Smears of material from the mouth and gums showed no predominating organism. Spirochetes and fusiform bacilli were almost always absent from the localized lesions but were found quite commonly in smears taken from the swollen gums. Cervical adenitis of a well marked degree was noted in fourteen children, a palpable spleen in one and diarrhea in six. Five children had an accompanying herpes of the skin of the lip and two had paronychia with lesions which looked like herpes. Four also had pneumonia, one dysentery, one diphtheria and one influenza bacillus meningitis. The disease appeared to be self limited in nature and lasted from a few days to two weeks. Swabbings from the lesions in the mouth of twelve unselected patients were inoculated immediately onto the scarified cornea of a rabbit in order to prove the presence or absence of the virus of herpes. Typical herpetic vesicles developed within twenty-four to forty-eight hours followed by a purulent keratoconjunctivitis. Usually the virus was transferred to a second rabbit, which was killed at the end of twenty-four hours. Immunity was demonstrated in six of seven rabbits which survived the infection.

Laryngoscope, St. Louis

48: 1-76 (Jan.) 1938

Some Cases of Otolaryngologic Interest That Were Seen on Neurologic Service. P. Northington, New York.—p. 1.
Abscess of Epiglottis: Report of Two Cases. G. M. Coates, B. H. Shuster and W. Gordon, Philadelphia.—p. 12.
Sinuses as Points of Focal Infection and Treatment of Sinusitis. W. Fletcher, Salem, Wis.—p. 17.
Osteoma of Sinuses. M. S. Ersner and M. Saltzman, Philadelphia.—p. 29.
*Low-Grade Fever: Result of Nasopharyngeal Infection. T. P. O'Connor, Chicago.—p. 38.
Atresia of Choana: Report of Case. J. H. Childrey, San Francisco.—p. 51.
Use of Sulfanilamide in Acute Mastoiditis: Report of Case. M. Vaisberg, Patchogue, N. Y.—p. 54.
Streptococcus Haemolyticus Meningitis with Recovery Following Use of Sulfanilamide: Two Cases. D. E. Godwin, Long Beach, Calif.—p. 59.
Deafness in the College Age. M. M. Kafka, Brooklyn.—p. 65.
Hearing Tests in an Iowa County. W. H. Gardner, Ottumwa, Iowa.—p. 69.

Nasopharyngeal Infection.—O'Connor discusses fifty-five cases of nasopharyngeal infection. The three most common complaints, in addition to fever and fatigue, were headache, loss of weight and aching of muscles. Thirteen of the patients were

known to have had a persistent leukocytosis and one patient had leukopenia. The ages of the group varied from 5 to 57 years. The duration of symptoms before patients were seen ranged from two weeks to seven years. There was no evidence of sinus infection except in four patients. The turbinal mucosa appeared perfectly normal. No secretion was present in the region of the natural orifices of the accessory sinuses. Transillumination of the maxillary sinuses was brilliant. X-ray studies of the sinuses, made in the majority of cases, were normal. Thirteen showed evidence of chronic but slight infection of the tonsils and 25 per cent showed hypertrophy of the lateral wall of the pharynx. The ears, structures of the nose and larynx were without significant abnormalities in all the cases. Inflammation of the nasopharynx of varying degree was found. In many cases it was localized in the remains of the pharyngeal tonsil. In others a diffuse inflammation of the whole nasopharyngeal area was present. A third group showed a localized inflammatory area on one wall or the other. A cultural study in most of the cases confirmed the presence of definite infection. While the bacteriologic studies confirmed the clinical and physical observations in the majority of cases, there were some that did not coincide. The infection may be situated deep in the tissue so that the responsible bacteria are not obtained in a culture taken from the surface. The symptoms may disappear when drainage is enhanced or absorption decreased, even though organisms still are present in large numbers. The cultures were particularly valuable in determining the type of treatment to be used, since dyes and other germicidal agents vary markedly in their effect on different bacteria. The local treatment consisted of direct application to the involved area of a solution of silver nitrate of varying strength, depending on the degree of congestion, or, in some instances, of a weak solution of zinc sulfate. This was followed by generous application of a 2 per cent aqueous gentian violet solution or a 2 per cent solution of methylene blue. When there was no response to this treatment, a 0.5 per cent solution of colloidal iodine was used, followed by the dye, and when there was no relief an autogenous filtrate was made, combined with a water soluble base and applied directly to the area. Usually, during the course of local treatment, the patient was instructed to use saline irrigations and mildly antiseptic drops. The number of treatments required to clear up the infection was dependent on the species of organism present. In most cases the focus was eradicated with from six to twelve treatments. Nine of the fifty-five patients failed to respond to treatment. Patients who do respond may be subject to reinfection with return of symptoms but then respond to treatment much more readily than in the initial attack.

Military Surgeon, Washington, D. C.

82: 81-184 (Feb.) 1938

Some Aspects of the Modern Concept of Orthodontics. L. C. Fairbank.—p. 81.
Fleet Medicine. G. F. Cottle.—p. 91.
Cardiovascular Disease in Neuropsychiatric Patients. B. A. Moxness.—p. 97.
Communications in the Medical Regiment. W. P. Davenport.—p. 107.
Report on Treatment of Dermatitis Venenata During the Season of 1937 at Fort Washington, Md. S. W. French.—p. 127.
The Training Schedule of the Eighth Medical Regiment, R. A. I. M. Kasich.—p. 131.
Neuritis Following Serum Administration. R. J. Hoagland.—p. 134.

Missouri State Medical Assn. Journal, St. Louis

35: 29-68 (Feb.) 1938

Accurate Differential Section for Treatment of Trigeminal Neuralgia. R. M. Klemme, St. Louis.—p. 29.
*Treatment of Staphylococcic Septicemia with Specific Antitoxin. H. M. Parker, Kansas City.—p. 30.
Coronary Thrombosis in Young Adults: Report of Case in Man Aged 30. M. S. Franklin, St. Louis.—p. 32.
Modern Advances in Treatment of Sepsis. H. Allen, St. Louis.—p. 35.
Function of the Child Welfare Program in Missouri. O. F. Bradford, Columbia.—p. 37.
Function of the Maternal Welfare Program in the State of Missouri. P. F. Fletcher, St. Louis.—p. 38.
Review of Idiopathic Ulcerative Colitis: Report of Five Cases. J. C. Kopelowitz, Los Angeles.—p. 41.

Staphylococcic Septicemia Treated with Antitoxin.—In a review of the four cases that Parker presents, certain salient features deserve especial mention. The treatment of staphylococcic septicemia is far from satisfactory. General supportive measures, transfusions at frequent intervals and the drainage of free pus whenever found still remain the foundation of all successful therapy in these infections. In each of these four cases such measures were instituted and in each instance the clinical course justified the conclusion that the early death of the patient was only a matter of time. Staphylococcus antitoxin was then added to the program, with brilliant results in three of the four cases. The cardinal features of severe staphylococcic infections were present in these cases. A rapidly progressive anemia requiring frequent transfusions, the phenomenon of venous thrombosis, the ultimate dissolution of the thrombus with septicemia, tissue invasion, toxemia, pulmonary metastasis and the like are readily explained in terms of a pyogenic organism with an exotoxin which is hemolytic, dermonecrotic, thrombophlebitic and, in sufficient dosage, lethal. The thrombophlebitis must be regarded as an essentially protective mechanism on the part of the host.

Nebraska State Medical Journal, Lincoln

23: 41-80 (Feb.) 1938

Electrocoagulation Treatment for Inoperable Carcinoma of Rectum. W. F. Bowers, Minneapolis.—p. 41.
Emergency Treatment of Fractures of Spinal Column. J. E. M. Thomson, Lincoln.—p. 45.
Compression Fractures of Body of Vertebra. W. L. Sucha, Omaha.—p. 47.
Some Recent Advances in Female Endocrinology. C. S. Moran, Omaha.—p. 51.
Management of Infection and Gangrene of Extremities in the Diabetic. M. Grodinsky, Omaha.—p. 54.
Public Health Aspects of a Nebraska Milk Supply: III. J. D. Le Mar and M. F. Gunderson, Omaha.—p. 59.
Use of Cystometer in Diagnosis of Neurogenic Bladders (with Comments on Treatment and Case Reports). P. S. Adams, Omaha.—p. 63.

New England Journal of Medicine, Boston

218: 143-204 (Jan. 27) 1938

Facts and Issues Regarding Public Medical Care. M. M. Davis, New York.—p. 143.
Gastroduodenal Ulcer: Etiology, Treatment and End Results. B. B. Crohn, New York.—p. 148.
Cerebral Arteriosclerosis: Vice Presidential Address. W. J. Upton, Burlington, Vt.—p. 157.
Carcinoma of the Colon: Study of Seventy Cases. D. S. Adams, Worcester, Mass.—p. 160.
*New Conception of Serum Phosphatase: Review of Experimental Work. S. Maddock, S. J. Thannhauser, M. Reichel and J. Grattan, Boston.—p. 166.
Use of Combined Pontocaine and Novocain for Spinal Anesthesia. S. C. Wiggin and J. Tartakoff, Boston.—p. 170.
Thrombo-Angiitis Obliterans of Spermatic Cord. J. Tartakoff and J. B. Hazard, Boston.—p. 173.
Coronary Occlusion in a Young Adult. D. Halbersleben, Boston.—p. 175.

Serum Phosphatase.—In attempting to explain the mechanism involved in the elevation of serum phosphatase in pathologic conditions, Maddock and his associates find that the most significant conclusion of clinical import that can be drawn from previous experiments is that what has always been regarded as an increase in amount of serum phosphatase in disease is not an actual increase in enzyme but merely an activation of preexisting enzyme normally present. This necessitates an alteration in the fundamental concept of phosphatase in both normal and pathologic states. The relation of serum phosphatase and bone phosphatase to the growth and repair of bone may well be involved. The mechanism of increased serum phosphatase in jaundice seems to be understandable in that any obstruction to the excretion of bile results in the damming up of both depressing (bile acids) and activating (cofactor) substances. Since the cofactor is more powerful as an activating agent than bile acids are as depressors, the net result is an increase in activity of serum phosphatase. The difficulty of attempting to use phosphatase determinations in the differential diagnosis of liver disease is thus apparent. Phosphatase activity must represent the outcome of reactions in a complex system consisting of enzyme, cofactor, oxidation-reduction potential and substrate. Thus the phenomenon is analogous to the cozymase system described by Warburg and von Euler. Human disease may originate from disturbances in enzymatic activity either from a deficiency or from an excess of any of the factors in the system.

Northwest Medicine, Seattle

37: 1-32 (Jan.) 1938

Psychologic Factors in Physical Disease. E. M. Burns, Portland, Ore.—p. 1.

Pathologic Physiology and the Psychoneuroses. W. Marshall, Appleton, Wis.—p. 5.

Study in Pseudoheredity: Cyclic Interrelationship of Juvenile Neuropathic Traits and Adult Tension Character in Successive Generations. A. W. Hackfield, Seattle.—p. 9.

Food History and Skin Sensitivity. M. W. Moore, Portland, Ore.—p. 12.

Nucleus Pulposus and Hypertrophy of Ligamentum Flavum: Case Reports. P. G. Flothow, Seattle.—p. 14.

Fracture of Neck of Scapula. M. R. Charlton, Tillamook, Ore.—p. 18.

Appendicitis in Children. C. W. Brunkow, Portland, Ore., and H. Currin, Klamath Falls, Ore.—p. 21.

Oklahoma State Medical Assn. Journal, McAlester

31: 1-32 (Jan.) 1938

Abortion: A National Health Problem. Gertrude Nielsen, Norman.—p. 1.

Congenital Hypertrophic Pyloric Stenosis. F. A. Glass, Tulsa.—p. 4.

Clinical Labyrinthitis. T. G. Wails, Oklahoma City.—p. 6.

Insulin Shock Therapy: Results to Date. G. W. Robinson Jr., Kansas City, Mo.—p. 9.

Fractures of Lower End of Humerus in Children. J. E. McDonald, Tulsa.—p. 12.

Abdominal Pain During Pregnancy. M. J. Serwer, Oklahoma City.—p. 15.

Pennsylvania Medical Journal, Harrisburg

41: 261-344 (Jan.) 1938

Laryngectomy: Its Place in Treatment of Laryngeal Cancer. L. A. Schall, Boston.—p. 261.

Pulmonary Disease Complicating Syphilis, Frank or Masked. H. F. Robertson, Philadelphia.—p. 267.

Pulmonary Emphysema. G. M. Piersol, Philadelphia.—p. 269.

Bronchoscopic Treatment of Pulmonary Suppuration, with Especial Reference to Use of Polyvalent Stock Bacteriophage. W. F. Moore, Philadelphia.—p. 272.

Surgical Treatment of Bronchiectasis. J. B. Flick, Philadelphia.—p. 274.

Pneumonia Control: Plan for Pennsylvania. Edith MacBride-Dexter, Harrisburg, and E. L. Bortz, Philadelphia.—p. 279.

Serum Treatment of Pneumonia. V. B. Callomon, Pittsburgh.—p. 283.

Relation of Nasal Sinus Infection to Involvement of Lower Respiratory Tract. G. L. Whelan, Philadelphia.—p. 287.

Some Practical Experiences with Contact Lenses. A. G. Fewell, Philadelphia.—p. 292.

Malignant Growths of the Thyroid. S. J. Waterworth, Clearfield.—p. 295.

Southwestern Medicine, Phoenix, Ariz.

22: 1-40 (Jan.) 1938

Orthopedic Aspects of Pain in the Lower Back. L. W. Breck, El Paso, Texas.—p. 1.

Treatment of Chronic Suppurative Otitis Media. C. Gwinn, Albuquerque, N. M.—p. 4.

Avertin (Tribrom-Ethanol) as Basal Anesthetic. W. J. Pangman, El Paso, Texas.—p. 6.

*Purpura Haemorrhagica Fulminans. H. S. Denninger, Glendale, Ariz.—p. 8.

Mastoiditis with Brain Abscess. J. L. Johnson, Phoenix, Ariz.—p. 10.

Traumatic Emergency Surgery. C. P. Austin, Douglas, Ariz.—p. 11.

Fulminating Hemorrhagic Purpura.—Denninger discusses two cases of fulminating hemorrhagic purpura. The cases were strikingly similar and suggest a possible familial tendency. The one occurred in a male child of 3 and the other in his aunt of 16 years. The etiology was doubtful; thrombocytopenia was suggested. In the child the first symptom occurred about 4 o'clock in the morning and was followed by death in eleven hours. In the second patient, evidence of definite symptoms started at 5 o'clock in the morning and had a lethal termination eight and one-fourth hours later. Signs of cerebral irritation (hemorrhage) were prominent in both as judged by pupillary reaction, clonic and tonic spasms, vomiting and diffuse abnormal body sensations. Scurvy may be ruled out on the basis that there was no evidence of dietary deficiency and the absence of large hematomas under the peritoneum or in the deep muscles of the body. Poisoning or drug reactions also were eliminated. Blood studies revealed nothing abnormal, indicating that a deranged thrombogenic mechanism was present and that these cases belong in the category of the true idiopathic purpuras of unknown etiology.

Surgery, St. Louis

3: 1-164 (Jan.) 1938

Operative Treatment of Scars Following Bedsores. J. S. Davis, Baltimore.—p. 1.

Acromegaly: Detailed Report on Two Cases. C. P. G. Wakeley and F. R. B. Atkinson, London, England.—p. 8.

Osteomyelitis of Scapula. A. O. Wilensky, New York.—p. 21.

Granuloma Venereum (Granuloma Inguinale) of Uterus, Tubes and Ovaries. E. R. Pund and V. A. Gotcher, Augusta, Ga.—p. 34.

*Lymphopathia Venereum: Treatment with Diluted Frei Antigen Intradermally and Observations on Diagnosis. O. L. Anderson and O. Harmos, Norfolk, Va.—p. 41.

*Cause of Death in Liver Peritonitis: Nature of Toxic Substances Produced by Incubation of Adult Dog Liver. H. E. Martin and H. M. Trusler, Indianapolis.—p. 58.

Large Bilateral Adenofibromas of the Breast: Report of Case in a Girl Thirteen Years of Age. G. Crile Jr., Cleveland.—p. 68.

Stenosis of Large Bowel Due to Amebiasis: Report of Case Treated by Extensive Resection. F. Christopher, Evanston, Ill.—p. 75.

Diaphragmatic Hernia in Infants: Surgical Treatment with Use of Renal Fascia. J. Weinberg, Omaha.—p. 78.

Effect of Anesthesia on Hepatic Function. F. P. Coleman, Ann Arbor, Mich.—p. 87.

Choice of Anesthetic Agents and Methods of Their Administration for Diabetic Patients. D. E. Hale, Butte, Mont., and R. M. Tovell, Hartford, Conn.—p. 100.

Acute Appendicitis. A. Strauss and J. Tomarkin, Cleveland.—p. 111.

Bone Metastases from Carcinoma of Stomach. S. E. Lawton, Chicago.—p. 121.

Effect of Carbon Arc Radiation on Wound Healing. H. M. Sweeney, New Orleans.—p. 127.

Treatment of Venereal Lymphogranuloma with Diluted Frei Antigen.—In fifty-four cases which gave positive Frei reactions, there were only three without characteristic clinical signs and history. Accordingly Anderson and Harmos have found the Frei test to be specific in 94.5 per cent. They observed discrepancies in certain cases when tested by various potent Frei antigens, also some differences in the microscopic appearance, which seem to support the opinion that there are at least two subgroups of the disease. The treatment in their forty-eight cases of venereal lymphogranuloma is presented. They feel that the use of diluted Frei antigen, administered intradermally, has demonstrated encouraging results and that its use should be continued with further study. The use of Frei antigen as a vaccine in treatment was not familiar to them in November 1935, when they began this type of treatment at the Norfolk Marine Hospital. They decided on the intradermal administration of the vaccine as a route more effective than subcutaneous or intravenous treatments. The sterile and potent Frei antigen, diluted four times, was found an effective agent in treatment. The resulting vaccine has been a 1:24 or 1:28 dilution of the heat treated pus in physiologic solution of sodium chloride. This diluted Frei antigen is the only type of treatment received by the authors' lymphogranuloma patients, plus occasional lymphadenectomy, incision and drainage. They administer the diluted antigen on the nonhairy surfaces of the thighs, at intervals of five days. The initial dose is 0.05 cc., which is increased at each dose by 0.05 cc. up to the maximal dose of 1 cc. The treatment is continued until the sinuses heal and the adenopathy subsides; or, in case lymphadenectomy was performed, until the wound heals, requiring from six to twelve doses of the vaccine. In general, the clinical response to the vaccines consisted of gradual reduction in the size of the gland to only a small indurated area within a period of from one to two months. The treatment prevented the formation of new fistulas, induced within a week a beginning reduction in the size of the glandular enlargement, and materially shortened the time required to close an operative wound.

Death in Liver Peritonitis.—Martin and Trusler believe that the putrefactive pressor bases, tyramine, iso-amylamine, phenolethylamine and histamine-like substances, are rapidly produced by the action of bacteria on liver substances during the process of incubation. Whether or not the amines with pressor effects on the blood pressure predominate over the amines with depressor effects depends on the kind of bacteria present in the digests. These toxic amines and other heat-stable, water-soluble, toxic substances formed in the process of incubation of dog liver were lethal when the equivalent of 200 to 300 Gm. of incubated liver was given slowly intravenously to an anesthetized dog. When injected intravenously into a

dog without anesthesia, the equivalent of 100 Gm. of incubated liver was sufficient to cause rapid death. The terminal event is convulsive seizures. In addition to other factors, putrefactive amines may also contribute to the rapid death of dogs subjected to liver peritonitis. It is conceivable that deep-seated infections in human subjects may give rise to toxic amines which enter the general circulation and contribute to the shock syndrome frequently associated with such infections.

Surgery, Gynecology and Obstetrics, Chicago

66: 129-256 (Feb. 1) 1938

Clinical Behavior of Early Carcinoma of Cervix. W. Schiller, New York.—p. 129.
*Cutaneous Healing in Wounds: Notes. J. H. Conway, New York.—p. 140.
Rate of Emptying of Human Gallbladder in Pregnancy. Maude M. Gerdes and E. A. Boyden, Minneapolis.—p. 145.
Krukenberg Tumors of Ovary: Clinical and Pathologic Study of Twenty-One Cases. E. Novak and L. A. Gray, Baltimore.—p. 157.
Study of Appendicitis: Analysis of 1,463 Consecutive Cases. E. W. Sprague, R. A. Schaaf, C. MacArthur, S. Z. Hawkes, H. Hantman and P. W. Haley, Newark, N. J.—p. 166.
Relation of Cartilage to Repair of Bone. J. D. Bisgard and J. M. Farris, Omaha.—p. 173.
*Inexhaustible Source of Blood for Transfusion and Its Preservation: Preliminary Report. J. R. Goodall, F. O. Anderson, G. T. Altimas and F. L. MacPhail, Montreal.—p. 176.
Obstetric Anesthesia: I. Laboratory Method for Studying Effects of Anesthetic and Analgesic Agents on Both Uterus and Fetus. B. E. Monar and C. M. Blumenfeld, Salt Lake City.—p. 179.
Inguinal Hernia: I. Anatomy of the Region. B. J. Anson and C. B. McVay, Chicago.—p. 186.
Id.: II. Surgical Treatment of Direct Inguinal Hernia. L. M. Zimmerman, Chicago.—p. 193.
*Total Tendon Transplant for Slipping Patella: New Operation for Recurrent Dislocation of Patella. E. D. W. Hauser, Chicago.—p. 199.
Segmental Enteritis. R. Lewisohn, New York.—p. 215.
Impalement of Rectum. F. M. Conway, New York.—p. 222.
Evipal Soluble: Basal Anesthesia. M. L. Weinstein, Chicago.—p. 227.
Pilonidal Cysts. S. A. Zieman, Chicago.—p. 231.
Thrombophlebitis of Varicose Veins. E. A. Edwards, Boston.—p. 236.
A New McDonald's Solution. E. McDonald, Philadelphia.—p. 246.

Cutaneous Healing in Wounds.—Conway declares that for a surgical incision and suture to have a direct effect on the degree of fibroblastic response in a clean incised wound and also on the ultimate cosmetic result the incision should be made parallel to Langer's lines of elasticity of the skin. In operations about the face and neck, the direction of these lines of elasticity is easily observed since they can be defined through facial grimace. However, in operations on the abdomen and extremities, primary importance is attached to exposure of the wound and attention rarely is paid to the direction of the incision as regards cutaneous tension. It is important to hold the skin taut while it is being incised so that incision may be made sharply at a right angle to the flat cutaneous surface. If this is not done the operator may divide the layers of the skin in an oblique plane—the so-called beveled incision. It is difficult to suture accurately the edges of such an incision in close approximation. When fine arterial silk threaded on small straight needles of the milliner's type is applied with the on-end mattress stitch, ideal approximation of the cutaneous margins may be achieved. Crêpe lisse dressing as advocated by Halsted impregnated with collodion and applied directly to the surface of the skin or, if the wound is not healed completely, over a layer of silver foil is an invaluable aid in limiting the stress on a sutured wound when it is in the early stages of healing and before its maximal tensile strength has been reached.

Placental Blood for Transfusion.—Goodall and his associates find that the placental blood furnishes an unfailing source of supply for transfusion. When the baby is born it is laid on the mother's abdomen. The cord is tied or clamped and wiped clean with a sponge moistened in 75 per cent alcohol. The cord is stripped free from blood for about 6 inches. The cord is cut with sterile scissors and the severed end is lowered below the vulva. A special towel with a 2 inch hole in its center is put over the hand, holding the cord in such a manner that the hand is opposite the hole. The towel is clamped to the operator's gown near the elbow with an Allis forceps. The end of the cord is passed through the aperture in the towel and so placed that its end hangs in the funnel of the receptacle held by the nurse. Pressure on the cord is then released completely and the blood is collected. Pressure on the fundus by the nurse or assistant hastens the emptying of the placenta. When completed, the cord is clamped. The process occupies about three minutes, and the average amount collected from each patient may vary from 100 to 150 cc. Blood grouping and Wassermann reactions receive due consideration and blood is always available when it is needed for transfusion. The preservative (suitable for sixty days) that has been found to be most suitable is that proposed by the Moscow Institute of Haematology and consists of 7 Gm. of sodium chloride, 5 Gm. of sodium citrate, 0.2 Gm. of potassium chloride, 0.004 Gm. of magnesium sulfate and 1,000 cc. of twice distilled water. The solution is put up in ampules of 25 cc., which gives the proper dilution when added to 100 cc. of distilled water. The preservative and blood from each case are mixed in approximately equal proportions. Preserved blood has many advantages over fresh blood. Food and other extraneous allergic reactions are eliminated. Certain individuals absorb a large quantity of unsplit proteins during digestion and these are capable of being neutralized by the allergins of that specific person, but the recipient may not be so fortunate, and, if not, an allergic reaction must follow. In preserved blood, autodigestion occurs and allergic reactions do not occur after forty-eight hours of preservation. Before transfusion, the fetal blood should be heated in a basin of water and shaken before transmission. It should be filtered through two layers of sterile gauze. Two or more fetal bloods may be given simultaneously, if necessary, after separate matching.

Tendon Transplant for Patella.—Hauser classifies and divides recurrent dislocations of the patella into three clinical types: congenital, traumatic and rachitic. An operation is described which is original in that it fulfils all the prerequisites of satisfactory correction: (1) it prevents recurrence of the dislocation, (2) it gives the patient a feeling of absolute security, (3) it reestablishes the functional capacity, (4) it gives the knee a normal appearance, (5) the risk to the patient is minimal and (6) the convalescence is short. Illustrative cases are reported. The method has been in use for five years and the results have been uniformly satisfactory. The technic of the operation referred to is as follows: A curved incision is made, starting above the upper lateral margin of the patella, curving laterally around the patella and coming back to the midline about half an inch below the tubercle of the tibia. The skin is freed on both sides to expose the patella, the conjoined tendon and the patellar ligament. The patellar ligament is then dissected free down to its insertion. A block of bone about one-half inch square, including the attachment of the patellar ligament, is removed from the tibia by means of the electrical saw on three surfaces and an osteotome on the upper surface under the ligament. The entire lateral side of the patella is then dissected free by dividing the fascia down to the capsule. The dissection is carried along the lateral side of the conjoined tendon, well up into the area of the fascia lateral to the vastus muscle; this thickened fascia is divided down to the capsule but the operation remains extra-articular. The patella can now be drawn medially. The insertion of the patellar ligament is drawn to the median side of the tibia and distally until the patella lies low in the normal position between the condyles. The periosteum is incised to make two flaps, which are reflected. Then a bony block half an inch square is removed from the tibia in this area. The attachment of the patellar ligament and its block are countersunk in this space, and the periosteum is then sutured over the block. The second graft is fitted into the space at the tibial tubercle. Three sutures of No. 1 chromic catgut act as further stays to hold the medial side of the patellar ligament to the periosteum. The stretched medial fascia is then reefed in the region of the upper margin of the patella. The skin is closed. The fixation is held by means of a cast of plaster of paris for from ten to fourteen days. The sutures are removed at the end of this period, after which the quadriceps muscle can be massaged and weight bearing started, with the leg extended. The fourth week after the operation has been performed the knee can be flexed and the quadriceps muscle allowed to contract voluntarily. Free flexion is permitted after six weeks.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

Brain, London

60: 377-564 (Dec.) 1937

Epilepsy: Paroxysmal Cerebral Dysrhythmia. F. A. Gibbs, E. L. Gibbs and W. G. Lennox.—p. 377.

Somatic Motor and Sensory Representation in Cerebral Cortex of Man as Studied by Electrical Stimulation. W. Penfield and E. Boldrey. —p. 389.

*Compression of Chiasma, Optic Nerves and Optic Tracts by Intracranial Aneurysms. G. Jefferson.—p. 444.

Observations on Dystrophia Myotonica. O. Maas.—p. 498.

Exogenous Cellular Content of Neurohypophysis in Man Under Pathologic Conditions. H. J. Wade.—p. 525.

Hydrocephalic and Focal Cerebral Symptoms in Relation to Thrombophlebitis of Dural Sinuses and Cerebral Veins. C. P. Symonds.—p. 531.

Compression of Chiasma, Optic Nerves and Optic Tracts.—According to the clinical classification of Bramwell, intracranial aneurysms may present themselves as apoplectic and paralytic. It is with the latter only that Jefferson deals, and of these only with such as have affected the visual apparatus; that is, by compression of the optic tract, chiasma or optic nerve. Of fifty-three intracranial aneurysms there were sixteen of pure subarachnoid hemorrhage (with nothing to indicate the precise site of the aneurysm), nine aneurysms with paralysis of cranial nerves (usually the third nerve), sixteen saccular (nonfistulous) aneurysms of the internal carotid in the cavernous sinus and twelve basal aneurysms with disturbance of the visual pathways. These last twelve cases are reported after being grouped under four headings: (1) those interfering with the optic radiation and striate cortex, three cases; (2) those compressing the optic tract, one case; (3) those affecting the optic nerves, two cases, and (4) those involving the chiasma, six cases. Of the first group the sudden onset of the disorder and the nonprogressive nature of the clinical pictures leave no doubt that two are examples of thrombosis of the posterior cerebral artery and the third of thrombosis of some part of the middle cerebral. In all these cases the immediate clinical picture was that of subarachnoid hemorrhage. The pathology of the type of aneurysms under discussion seems in no way to differ from that of the so-called berry aneurysm. In general they occur like other aneurysms, at the bifurcation of a large vessel, in this case the internal carotid, perhaps where the ophthalmic artery leaves it or, in the suprachiasmal group, at the point where the anterior cerebrals are joined by the anterior communicating branch. The differential diagnosis of a chiasmal lesion rests on the nature of the field defect, coupled with the manner of its evolution and the rapidity of its development, the degree of pain associated with the evolution of the visual defect, the coexistence of other neurologic signs, the presence or absence of tuberal or endocrine disturbance and the x-ray evidence. There is only one useful treatment for these cases, and that is carotid ligation.

Journal of Tropical Medicine and Hygiene, London

41: 21-36 (Jan. 15) 1938

Diseases of Skin in Negroes. L. J. A. Loewenthal.—p. 21.

Blood Grouping of Aborigines of the Northern Flinders Ranges in South Australia. J. B. Cleland and T. H. Johnston.—p. 26.

Antimony Ointment and Antimony Rashes in Treatment of Bilharziasis. F. G. Cawston.—p. 27.

Lancet, London

1: 123-180 (Jan. 15) 1938

Nutrition and Nutritional Diseases: II. Role of Vitamin C in Disease. L. G. Parsons.—p. 123.

Effect of Estrogenic and Other Sex Hormones on Response of Rat to Vasopressin. F. B. Byrom.—p. 129.

Cavernous Hemangioma of Orbit Successfully Removed by Krönlein's Operation. H. B. Stallard.—p. 131.

Normal Level of Plasma Bilirubin. Janet Maria Vaughan and G. A. D. Haslewood.—p. 133.

*The Heart in Diphtheria. H. M. Leete.—p. 136.

Outbreak of Acute Respiratory Infection in Neonatal Ward. Alice E. Dickie.—p. 139.

The Heart in Diphtheria.—The prevalence of severe diphtheria in Hull during the last six years has given opportunities for the observation and study of the toxic effects seen in this disease. Leete attempts to classify the varying degrees of myocardial damage with a view to prognosis and management of the cases, based on a series of 4,700 cases of faucial diphtheria, which included 461 deaths, mostly toxic, and 452 cases of nonfatal paralysis. The large number of toxic deaths is due chiefly to the high incidence of virulent strains of Corynebacterium diphtheriae during this time. The majority of toxic deaths occurred within the first fifteen days of disease. In all these cases the heart is undoubtedly affected, but when death occurs early, during the first week, cardiac phenomena are not prominent and are so overshadowed by the general poisoning that one is inclined to say that these early deaths are due to general toxemia. Later, from the seventh to the fourteenth day of disease, cardiac symptoms and signs are more in evidence and the impression given is that death is due to cardiac or circulatory failure. Late cardiac deaths associated with paralyses in the fifth and sixth week have not been seen. Cardiac signs are slight and similar to those encountered in any very severe toxemia. Severe cases will certainly necessitate seven, eight or even twelve weeks in bed and this treatment must be given. But mild and moderate cases that have not given the indications of toxemia require no further treatment by the end of the fourth week and the patients may safely be sent home. Absolute rest is still all important in the cardiotoxic cases. Whether any drug influences this condition for good is open to doubt. Survival depends on the amount and distribution of undamaged or lesser damaged myocardial tissue and it is difficult to see how the stimulation of this modicum is helpful. Conservation should be the aim; the control of vomiting in toxic cases by dextrose and insulin, and the careful use of morphine to secure the all important rest are indirect methods of cardiac treatment that mean more to the patient than any cardiac drugs.

Medical Journal of Australia, Sydney

1: 47-90 (Jan. 8) 1938

Certain Modern Agents for Detection and Abolition of Susceptibility to Diphtheria. C. W. Adey.—p. 47.

Diphtheria Immunization. J. M. Dwyer.—p. 52.

Types of Corynebacterium Diphtheriae Prevalent in Victoria and Their Clinical Significance. T. S. Gregory.—p. 57.

Immunity Studies in Diphtheria. H. L. Carruthers.—p. 59.

Use of Molds and Surface Applicators in Radium Therapy. H. J. Ham. —p. 62.

Creatine Retention in Blood and Cerebrospinal Fluid. A. Bolliger and A. L. Carrodus.—p. 69.

Strangulated Hernia. R. H. Fulton.—p. 73.

South African Medical Journal, Cape Town

12: 1-40 (Jan. 8) 1938

Medicine and Politics. K. Bremer.—p. 3.

Inflammation of Entrance to the Orbit. W. P. C. Zeeman.—p. 5.

Puerperal Sepsis at Home and in the Hospital. R. Theron.—p. 9.

The Chest Lead in Electrocardiography. B. Cohen.—p. 14.

Japanese Journal of Experimental Medicine, Tokyo

15: 355-416 (Dec. 20) 1937

Experimental Studies on Metabolism of Urea. T. Saitô.—p. 355.

Contribution to the Histopathologic Examination of Experimental Syphilis and Yaws in Rabbits. H. Takahasi.—p. 401.

*Supplemental Studies on Virus of Lymphogranuloma Inguinale: I. Virulicidin of Immune Serum of Rabbits. J. Okanishi.—p. 407.

Id.: II. Existence of Virus in Cerebrospinal Fluid of Infected Mice. J. Okanishi and E. G. Vio.—p. 413.

Virus of Venereal Lymphogranuloma.—Okanishi finds that the cerebrospinal fluid of mice infected with the virus of venereal lymphogranuloma is turbid and viscous. It contains numerous cells, from 2,000 to 4,000 in 1 cc. of fluid, most of which are lymphocytes. The brains of infected mice were washed with sterile saline solution, and the supernatant fluid was obtained by centrifugation of the washing. Even the intracerebral inoculation of the fluid in a dilution of 1:10,000 into healthy mice caused the typical symptoms of the disease to appear, which fact shows that the supernatant fluid contained the virus in abundance. This method of obtaining the fluid almost free from impurities, yet with a high content of the virus, will greatly aid in the investigations on the virus of this disease.

Presse Médicale, Paris

46: 209-224 (Feb. 9) 1938

Limits of Prevention of Tuberculosis in Human Species by Means of Calmette-Guérin Vaccine. B. Weill-Hallé.—p. 209.

*Treatment of Painful Crisis of Gastroduodenal Ulcer by Small Doses of Histamine. A. Jacob and L. Israel.—p. 210.

Histamine in Treatment of Painful Crisis of Gastric Ulcer.—Jacob and Israel direct attention to the histidine treatment of ulcers of the digestive tract which was introduced by Weiss and Aron. After reviewing the theory of histidine deficiency, on which this treatment is based, they show that the ampules of 4 per cent solution of histidine which were utilized for the treatment of gastric ulcers betwen 1933 and 1935 contained traces of histamine. Because there were indications that these traces of histamine, approximately 0.1 mg. per ampule, were the effective factor, the author resorted to the subcutaneous injection of 0.1 mg. of histamine in patients with ulcers of the digestive tract. They report the clinical histories of seventeen of the thirty-eight patients with gastric ulcer in whom they employed the daily injection of 0.1 mg. of histamine. The histories indicate that the usual number of injections was ten; in some the number was smaller and in others it was larger. In all these cases the pain of the ulcer disappeared, often after the third injection. Discussing the mode of action of the histamine treatment, the authors mention the vasodilatory effect on the capillary system in general, and particularly on that of the gastrointestinal tract, the contracting action on the smooth muscles of the digestive tract and the remarkable antalgic power of histamine. They point out further that, if histamine is so effective against the painful crises of ulcer, it is likely that it exerts also a therapeutic action on the ulcer itself. They think that a cicatrization of the ulcer might be possible but insist that so far this is still in the domain of hypothesis.

Cuore e Circolazione, Rome

22: 1-60 (Jan.) 1938

Velocity of Circulation in Heart Diseases. T. Sessa.—p. 2.

*Treatment of Heart Diseases by Antithyroid Roentgen Therapy. T. Galli.—p. 32.

*Relation Between Velocity of Circulation and Basal Metabolism in Heart Diseases. E. Ascarelli.—p. 44.

Treatment of Heart Diseases by Roentgen Therapy of Thyroid Region.—Galli states that roentgen irradiations of the thyroid region give better results than thyroidectomy in the treatment of heart diseases. The treatment induces a controllable diminishing hypofunction of the thyroids with consequent improvement of the cardiovascular function and of the decompensation of the heart. It is harmless and not followed by myxedema. In administering the irradiations he divides the thyroid region into three imaginary fields which correspond to the right and left lobes and to the isthmus. The irradiations are given through a filter of 0.5 mm. of zinc and 2 mm. of aluminum. The first six treatments are given daily. The second six are given every other day. Only one field is irradiated at a time. The treatments are given in succession to the first, second and third fields at a dose of 300 roentgens for each irradiation. The first and second series of six treatments each are followed by a period of temporary discontinuation for two or four weeks, according to the absence or appearance of an erythematous reaction and then repeated by the same technic up to a total, which varies from three to four series. If the patient suffers from cutaneous hypersensitivity the treatments are given at longer intervals. The author has treated several cases, one of which is reported. Up to the present, three months after discontinuance of the treatment, the satisfactory results obtained are lasting. The article is a preliminary note.

Relation Between Velocity of Circulation and Basal Metabolism in Heart Diseases.—Ascarelli determined the velocity of circulation and the basal metabolism of fifty-eight patients who were suffering from heart diseases. In decompensated heart diseases the velocity of circulation is diminished and the basal metabolism is increased. The variations are proportional to the intensity of decompensation. However, there are frequent exceptions. An increase or diminution of the basal metabolism which is proportional to those of the velocity of circulation shows better clinical conditions of the patients than the presence of a basal metabolism and a velocity of circulation which follow opposite directions in increase and decrease, respectively. The author searched for a direct proportional ratio of the tests and obtained a product which he calls coefficient of velocity of circulation and basal metabolism. The figures of the coefficient are proportional to the evolution of the clinical condition. The coefficient increases as the clinical conditions are aggravated and decreases as they improve. The coefficient is of prognostic value and more reliable for decompensation of the heart than the results of the velocity of circulation or of the basal metabolism by themselves.

Minerva Medica, Turin

1: 85-112 (Jan. 27) 1938

Malignant Epidemic Septicemia (M. E. S.) in Natives of Harrar. G. Ferro-Luzzi.—p. 85.

Functional Correlations of Various Segments of Digestive Tract and Their Relations to Endocrine Secretion of Pancreas. G. Cozzutti.—p. 90.

*Zambrini's Ptyaloreaction in Surgery. C. Scartozzi.—p. 99.

Zambrini's Ptyaloreaction in Surgery.—Zambrini's reaction for the diagnosis and prognosis of vital resistance, its technic and several of its applications have been described in various medical journals, especially French and Italian and in THE JOURNAL, Nov. 14, 1936, page 1679. The test is based on the changes of saliva produced by the addition of a coloring reagent and measured by a standard colorimetric scale. According to the literature, the color of saliva in the light shades (low figures in the scale) indicates a diminished vital resistance or poor evolution of the course of the disease, whereas dark shades (high figures in the scale) indicate good vital resistance and satisfactory evolution of the disease. Scartozzi made the test in fifty cases in which operation was to be performed. He found that before the operation the saliva of patients in normal condition, except for the presence of the surgical condition (hernia or varicocele), gives high figures in the colorimetric scale, while that of patients in poor nutritional and general condition or with disturbed crasis of the blood (appendicitis, gastroduodenal ulcer and cholecystitis) gives low figures in the scale. The immediate and following postoperative reactions of the patients do not show any relation to the figures given by the test before the operation. The figures in the chromatic scale diminish in all cases after the operation and return to preoperative figures in from three to five days after the operation unless local or general complications develop. There is no relation between the type of anesthesia used in the operation and the behavior of the vital resistance during and after it. The author concludes that Zambrini's test shows the actual vital resistance of the patient but does not have any prognostic value. The reaction takes place by deviations of the p_H of saliva from the neutral point to the acid or alkaline zones. Zambrini's fluid is an indicator. The p_H of normal saliva is in the alkaline zone in Zambrini's scale. A reaction showing increased acidity of saliva shows a tendency to acidosis and a diminished vital resistance. The reaction shows the actual but not the total acidity of saliva. The latter can be ascertained by the sensitivity of the p_H of the saliva to be displaced from one to another zone around the neutral point when a certain number of drops of decinormal solution of acids or bases, which varies from 1 to 14, is added to the saliva. The larger the number of drops that are necessary to displace the p_H of a given specimen of saliva, the more intense the total acidity of the saliva. According to the author the determination of total acidity of the saliva is of value in estimating the final results of the reaction for the vital resistance.

Policlinico, Rome

45: 225-268 (Feb. 7) 1938. Practical Section

*Test of Hippuric Acid in Liver Diseases. E. Ascarelli.—p. 225.

*Treatment of Echinococcic Cyst of Lung by Artificial Pneumothorax: Case. G. Roberti.—p. 233.

Hippuric Acid in Liver Diseases.—Ascarelli followed the behavior of the elimination of hippuric acid through the urine, during the first four hours subsequent to administration of 6 Gm. of sodium benzoate by mouth, as a test for function of the liver in synthetizing hippuric acid. He carried on the

test in ten normal persons and in forty-one patients who were suffering from liver diseases. He found that the total amount of hippuric acid eliminated in the urine of normal persons during the test is about 3 Gm. The amount of hippuric acid eliminated during the test by patients who are suffering from liver diseases with involvement of the liver parenchyma (toxic and hepatic jaundice, cancer or metastases of the liver and atrophic cirrhosis) is diminished. It is almost normal in patients who are suffering from diseases of the biliary tract, with or without jaundice, syphilis, with or without splenomegaly and jaundice, in certain forms of nonatrophic cirrhosis of the liver and in cardiac diseases with a stasic liver. The amount of hippuric acid eliminated during the test varies according to the improvement or aggravation of liver insufficiency. However, low figures of elimination of hippuric acid do not show a fatal evolution of liver diseases, as the results of the test show insufficiency only of the detoxicating function of the liver. The test is of an easy technic and of diagnostic and prognostic value. It is advisable to use it as a complementary test for the function of the liver.

Echinococcic Cyst of the Lung.—Roberti's patient, aged 18 years, showed clinical symptoms simulating tuberculosis. The roentgenograms of the lung were similar to those of cavitation of the tuberculous lung. The sputum gave negative results for tubercle bacilli. In the course of artificial pneumothorax an echinococcic cyst was eliminated during coughing. The patient gave positive results to the Casoni test. The air insufflations were followed several times by coughing and elimination of echinococcic membranes up to complete elimination of the cyst and recovery of the patient as collapse therapy took place.

Archiv für Gynäkologie, Berlin

165: 135-316 (Dec. 28) 1937. Partial Index

Estrogenic Hormone and Metaplasia of Pavement Epithelium of Mucosa of Corpus Uteri. F. Siegert.—p. 135.
Influence of Ovarian Function on Lactogenic Action of Hypophysis. M. Wiegand.—p. 149.
Preservation of Ovarian Function After Extirpation of Uterus. S. Siegmund.—p. 155.
*Significance of Achylic Chloranemia (Essential Hypochromic Anemia) in Gynecology. A. Hildebrandt.—p. 164.
Relations of Gonadotropic Action of Adrenal Cortex to Function of Gonads. F. Hoffmann.—p. 177.
Results of Functional Test of Lung During Pregnancy. W. Borgard and G. Effkemann.—p. 183.
Examination of Ovaries and Related Organs During Senility. J. Wallart and S. Scheidegger.—p. 189.

Significance of Achylic Chloranemia in Gynecology.—Hildebrandt thinks that knowledge about achylic chloranemia is not sufficiently disseminated and that the disorder does not receive the attention it deserves. The varying interpretation of the leading symptoms of the disorder are the reason why so many different terms have been applied to the disorder. In the German literature, achylic chloranemia and essential hypochromic anemia are the most commonly used terms. The disorder is much more frequent in women than in men. Most statistics agree that 80 per cent or more of the patients are women. It is said that the age groups between 30 and 50 years are most subject to it. The patients frequently complain of fatigue, lack of energy, palpitation, tinnitus aurium, attacks of fainting, painfulness of the bones, loss of weight and gastrointestinal disturbances, such as lack of appetite, flatulence, constipation or, more frequently, diarrhea. Other symptoms are burning sensations along the esophagus with difficulty in swallowing, burning of the tongue, paresthesias, particularly in the terminations of the extremities, and even slight disturbances in walking, all of which are symptoms that in a more severe form appear in pernicious anemia, to which achylic chloranemia seems related. The objective symptoms are likewise similar to those of pernicious anemia: there are changes in the lingual mucosa, trophic disturbances in the appendages of the skin, particularly of the nails, and rhagades. The skin is often pale white. The chief symptom of achylic chloranemia is a disturbance in the secretion of the gastric juice. Examination of the blood is of great importance for the diagnosis of the disease. The principal symptom is the hypochromia. The number of erythrocytes is often decreased. After pointing out that achylic chloranemia may be accompanied by circulatory disturbances, the author gives his attention to menstrual anomalies and genital hemorrhages that may appear during this type of anemia. He says that Schulten, on the basis of fifty cases, estimated the incidence of severe menstrual hemorrhages in achylic chloranemia at approximately 75 per cent. He himself, having observed only six cases, is unable to give definite percentages, but he gained the impression that menorrhagia and metrorrhagia not only occur in achylic chloranemia but may dominate the clinical picture. He describes the clinical histories of patients in whom this was the case, but he also says that menstrual anomalies were absent in two of the cases of achylic chloranemia that he observed. Iron therapy is the method of choice in achylic chloranemia. He administers reduced iron, giving 1 Gm. three times daily, and in order to intensify the action of the iron he also gives hydrochloric acid. The iron therapy must be continued until a considerable improvement is noticeable in the blood status. The menstrual disturbances or genital hemorrhages that may exist improve simultaneously with the blood status under the influence of the iron therapy.

Klinische Wochenschrift, Berlin

17: 1-40 (Jan. 1) 1938. Partial Index

Vitamin C Balance in Human Subjects. K. Wachholder.—p. 5.
Significance of Cutaneous Vessels for General Circulation. P. W. Springorum.—p. 11.
*Action of Sulfanilamide Compounds on Causal Organism of Gonorrhea. H. Felke.—p. 13.
*Pancreatropic Hormone of Anterior Hypophysis in Treatment of Acute Pancreatitis. O. Wustmann.—p. 16.
Therapy of Malignant Diphtheria with Vitamin C and Adrenal Cortex Extract. S. Werner.—p. 17.
Diagnosis of Septic Arterial Embolisms, with Especial Consideration of Conditions in Endocarditis Lenta. E. Ask-Upmark.—p. 20.
Electrocardiogram in Osteitis Fibrosa Cystica Generalisata (Recklinghausen). C. Korth and H. Hecht.—p. 21.

Action of Sulfanilamide in Gonorrhea.—Felke reports investigations that were conducted in order to explain the therapeutic action of some sulfanilamide preparations in gonorrhea. He finds that nearly all investigators agree that the pathogenic organisms are somehow impaired by the sulfanilamide and thus are made vulnerable for the defense powers of the organism. The sulfanilamide preparations that he used were several preparations identified by numbers. In summarizing, he says that the sulfanilamide compounds that are effective in the therapy of gonorrhea inhibit the growth of gonococci in the test tube when used in the same concentrations that are reached during the therapy in the organism. In some strains of gonococci there is no inhibition of growth with these concentrations, but considerably more sulfanilamide has to be added in order to inhibit growth. These sulfanilamide-fast strains of gonococci generally are derived from patients who are resistant to this chemotherapy. From the results of control cultures on patients it is concluded that this different behavior of the gonococci is a result of the immunity status of the organism. Strains of gonococci can be made sulfanilamide fast in culture experiments. Testing strains of gonococci obtained from patients in culture mediums that contain sulfanilamide preparations is occasionally helpful in deciding on the best chemotherapy.

Pancreatropic Hormone in Acute Pancreatitis.—After discussing the disturbances that exist in acute pancreatitis, Wustmann directs attention to the discovery by Anselmino and his associates of a pancreas-stimulating substance in the anterior lobe of the hypophysis. Inspecting microscopic preparations of the pancreas of animals that had been treated with the aforementioned pancreatropic hormone, the author observed a considerable hyperemia and reasoned that, if the pancreatropic substance has such an effect it might be helpful in acute pancreatitis. For the last four years he has endeavored to obtain clinical experience with regard to the course of acute pancreatitis when the pancreatropic anterior pituitary hormone was employed as an adjuvant in the treatment. As soon as a case has been diagnosed as pancreatitis, the patient is subjected to a continuous drop infusion of physiologic solution of sodium chloride. One ampule of the substance (as fresh as possible) is introduced into the injection tube every eight hours during

the first day. From the second day on, it is given every six hours in the form of tablets, until the fasting blood sugar and the diastase values have been normalized or until improvement is noticeable. The author employed this auxiliary endocrine treatment in nine patients with acute pancreatitis. The results were encouraging. The blood sugar and diastase values decreased rapidly, and necessary interventions on the biliary system could be made early.

Medizinische Klinik, Berlin

34: 1-35 (Jan. 7) 1938. Partial Index

Supposed Causes of Greater Incidence of Rickets in Recent Years. E. Rominger.—p. 1.
*Lichen Urticatus of Exogenic Origin. F. Hamburger and A. Dietrich.—p. 4.
Influence of Environment on Size of Heart. H. Stieve.—p. 5.
Does Specific Involvement of Regional Lymph Nodes Occur in Tertiary Syphilis? J. Zange.—p. 9.
New Methods in Treatment of Gonorrhea. H. Löhe, K. Schölzke and D. Zürn—p. 11.
*Trombidiosis. H. Aretz.—p. 15.
Hormone Treatment of Gonadal Insufficiency in Men, with Consideration of the Synthetic Testosteron-Propionate Perandren. R. Pick.—p. 17.

Lichen Urticatus of Exogenic Origin.—Hamburger and Dietrich say that lichen urticatus, which is comparatively frequent in children, is generally ascribed to enterogenic causes. Eggs, milk, meat and various types of vegetables have been held responsible for it, but the authors show that bites of insects, particularly bedbugs, are often responsible for this type of skin disorders. They were able to demonstrate that among twenty-four children with lichen urticatus there were seventeen, or 70 per cent, who reacted to bites from bedbugs with the characteristic manifestations of lichen urticatus. Tests on sixty-six children without lichen urticatus revealed that only twenty-four or 36 per cent, were sensitive to bites from bedbugs. In many cases of lichen urticatus the causal significance of bedbugs could be definitely demonstrated by the fact that the children had a recurrence immediately after their return home. However, this was not the case when the bedbugs had been exterminated or the children were taken to a home that was free from bedbugs. The authors point out that it is an old established fact that there are persons who have a sensitivity to bites from bedbugs and they think that for this reason it is the more surprising that for the last two or three decades lichen urticatus has been so generally ascribed to nutritional factors. In experimental studies they were never able to elicit lichen urticatus by foods. They do not question that a typical urticaria may be of enterogenic origin, but they doubt that lichen urticatus originates in this manner. They emphasize that lichen urticatus in children is not of enterogenic but rather of exogenic origin. In the majority of cases it is probably caused by bites from bedbugs, but fleas or other insects may also be responsible.

Trombidiosis.—Aretz says that trombidiosis is caused by mites of the genus Trombicula. The species Trombicula autumnalis seems to be the one which causes trombidiosis in Germany. Of the four developmental stages of the mite, only the larva lives above the ground and only the larva plays a part in the causation of trombidiosis. The larva is yellow to scarlet red; its length varies between 0.27 and 0.68 mm. and its width between 0.19 and 0.49 mm. It has three pairs of legs, the mandibular pair having especially powerful claws. The larva becomes a parasite on birds, mammalians or human subjects and with powerful mandibular claws penetrates the upper horny layer and introduces a salivary secretion, which transforms the upper layers in such a manner that they can serve as food. After sufficient food has been absorbed, the larva leaves the host. Experiments conducted by Fuhs and also by the author revealed that from three to four hours after the attack by the larva itching is felt, and a small papule, from 1 to 2 mm. in diameter, can be observed. Rubbing increases the itching. The papule becomes gradually larger and reaches its maximum after twenty-four hours. At the apex of the papule there may be a vesicle that is filled with clear fluid. After this vesicle dries up, a tiny blood crust is visible. The extremely slow regression of the papule, which requires about fourteen days, begins on the second or third day. In regions where the skin is delicate, the papules may become hemorrhagic. Itching persists until the papule has completely disappeared. Impairment of the general condition exists only in severe cases. To be sure, complications in the form of pyodermias may develop from scratching. Although severe forms of trombidiosis may develop in the tropics, the trombidiosis of the temperate zone has a favorable prognosis. The treatment is directed chiefly against the itching sensation. Application of soft (green) soap has been found helpful by Fuhs, von Mallinckrodt recommends a sulfur mixture and Hoffmann advises the use of ristin (ethyleneglycol monobenzoate) and a 20 per cent perugen ointment. The author obtained satisfactory results with frequent baths and with a simple zinc mixture. He describes the groups of cases that came under his observation.

Strahlentherapie, Berlin

60: 541-720 (Dec. 18) 1937. Partial Index

Actual Questions of Short Wave Therapy in Gynecology. I. von Kövesligethy-Büben.—p. 541.
*Experiments with Rotation Irradiation. F. Dessauer, K. Lion and M. Gökmen.—p. 645.
Dosimetry for Radium Packs. E. Hasché, J. Bolze, L. von Bozóky and D. von Keiser.—p. 598.
Gynecologic Short Wave Therapy. H. Korb.—p. 615.
Roentgen Irradiation of Benign Bone Diseases. W. Lahm.—p. 631.
*Foundations of Dosage in Rotation Irradiation. R. du Mesnil de Rochemont.—p. 648.
*Roentgen Therapy of Hyperthyroidism. W. von Wieser.—p. 712.

Rotation Irradiation.—Dessauer and his associates describe a method which makes it possible to apply greatly increased depth doses without increasing the doses that reach the skin and the covering layers. They admit that this method, namely, rotation irradiation, has been suggested several times before but has never been systematically developed. The authors experimented with this rotation method for the last two years and gained the impression that the improvement obtained with it is so considerable that, as soon as the rotation chairs have become available, the method will be employed. If, for instance, a complete focal dose can be applied to a tumor of the sella turcica without the hair falling out and if in case of a complete Coutard irradiation there is hardly any reaction of the skin, this is such a relief for patient and physician that it will not be dispensed with. The essential factor of rotation irradiation is to apply the total dose to the disease focus through as large a body surface as possible. To accomplish this the body of the patient is placed so that it can be rotated and adjusted in such a manner that the focus of the disease is in the axis of rotation. If the body of the patient is slowly rotated, the rays reach the focus of the disease uninterruptedly (because the focus remains within the axis), but the surface layers move so that the cone of rays constantly reaches different layers. Another advantage of the rotation method is that it permits a closer approach to the object to be irradiated and thus makes possible a better utilization of the ray energy, so that the irradiation time can be greatly reduced. The authors further discuss dosimetry, the structure of the apparatus and the technic of the irradiation by rotation.

Dosage in Rotation Irradiation.—Du Mesnil de Rochemont discusses the geometric factors in rotation irradiation and the spatial distribution of the dosage that is obtainable under different practical conditions. He emphasizes that this knowledge is the basis of the practical application of the rotation method of irradiation regardless of the manner in which the rotation is accomplished, whether, as was suggested by Dessauer and done by this author, the patient is rotated around the stationary x-ray tube or the x-ray tube is turned around the patient, as done by Flax. The distribution of the dose in the organism during rotation irradiation is determined by the difference in exposure time of the skin and of the focus at which the rays are directed. The author explains the computation of this difference in the time of exposure and clarifies the mathematical formulas used in this computation on a geometrical diagram. He also shows groups of curves that have been computed with these formulas and directs attention to the superior depth action and other advantages of rotation irradiation.

Roentgen Therapy of Hyperthyroidism.—According to von Wieser, roentgen therapy of hyperthyroidism is successful in only 60 to 70 per cent of the cases. He ascribes the considerable percentage of cases that fail to respond to roentgen treatment to the fact that, besides the primary form of hyper-

thyroidism, there are also secondary forms. There is one which develops as a sequel to cerebral disturbances in the sphere of the sympathetic nerve centers. In this connection he cites a case in which a previous lethargic encephalitis was the cause of a secondary hyperthyroidism. This case did not respond to irradiation of the thyroid, but as soon as the sympathetic centers in the brain were irradiated there was improvement. The author thinks that many failures of roentgen therapy in hyperthyroidism are due to the fact that the causes of the disorder have not been correctly recognized. He shows that a certain functional disturbance of the hypophysis resembles hyperthyroidism and that roentgen treatment of the thyroid fails in these cases. The fact that a number of such cases had been referred to him recently for irradiation of the thyroid induced him to discuss this problem. He says that, although these patients had an increased basal metabolism, their obesity should have suggested the possibility of an erroneous diagnosis. In all these cases, determination of the specific dynamic value had been neglected. If this had been done, it would have been discovered that the specific dynamic value was not increased as in hyperthyroidism but was decreased. The author mentions two other forms of secondary hyperthyroidism: that which results from infectious diseases, particularly tuberculosis, and that which is caused by excessive intake of thyroid extract or of iodine. The latter form usually improves when the intake of these substances is discontinued. In the concluding summary the author emphasizes once more that before roentgen treatment is begun in hyperthyroidism the cause of the disorder should be ascertained, for, if the process is one of the secondary forms, the treatment must be different than in the primary form. Roentgen irradiation of the thyroid is not effective in the secondary forms.

Zeitschrift für klinische Medizin, Berlin

133: 91-222 (Dec. 3) 1937. Partial Index

Sleep, Blood Sugar and Acid-Base Economy. C. Dienst and B. Winter. —p. 91.
Estimation of Changes in Electrocardiogram in Diseases of Myocardium. W. C. Meyer.—p. 105.
*Central Nervous Regulation of White Blood Picture: Studies on White Blood Picture After Spinal Puncture. C. H. Behr.—p. 132.
Vitamin A and Cholesterol Content in Its Relation to Elimination of Vitamin A in Urine: Demonstration of Vitamin A in Exudates, Duodenal Juice and Feces. F. Grant.—p. 168.
*Resistance to Insulin in Diabetes. R. Herbst.—p. 186.
*Action of Crystalline Insulin on Blood Pressure, Respiration and Electrocardiogram as Well as Modification of These Effects by Metrazol. A. Heinrich and Hildegard Sussner.—p. 208.

Central Regulation of White Blood Picture.—Behr reviews the literature on the central regulation of the white blood picture and then says that he observed that spinal puncture produces an increase in leukocytes. He believes that the degree and the type of changes in the white blood picture are to a certain extent dependent on the nature of the changes in the central nervous system. His observations were made in sixteen cases. The leukocytic blood picture was examined before, immediately after and twenty, forty and sixty minutes after the spinal puncture. The course of the leukocytic reaction and particularly the qualitative changes in the white blood picture permit a differentiation into three groups. To the first group belong four patients who had no pathologic changes in the central nervous system. The spinal puncture was made in order to verify the diagnosis. In these cases the spinal puncture produced only a slight increase in leukocytes. The second group, of four patients, had localized noninflammatory processes of the central nervous system. In this group the increase in leukocytes was more pronounced. It involved primarily the lymphocytes. The third group, of eight cases, included those in which the changes in the central nervous system could be traced to inflammatory infectious processes, especially of a syphilitic nature, and in which the meninges were involved. In these cases the spinal puncture was followed by a strong increase in leukocytes. The qualitative analysis of the blood picture revealed a deviation in the myeloid direction. The author considers these observations interesting, because the behavior of the leukocytic reaction after a spinal puncture permits some conclusions about the type of changes in the central nervous system. Inflammatory changes become manifest by a myeloid tendency in the leukocytic reaction, whereas purely degenerative processes are indicated by a noticeable lymphatic tendency in the leukocytic reaction. On the other hand, these observations seem to be a further proof for an autonomic regulation of the white blood picture. However, it is still a question whether a separate center exists for this regulation.

Resistance to Insulin in Diabetes.—A review of the literature on the resistance to insulin reveals no agreement about the nature of this phenomenon. The observations which Herbst made on the problem of resistance to insulin are based on sixteen cases. He emphasizes that the estimation of the efficacy of insulin cannot be based on the behavior of the blood sugar during fasting or on the total daily elimination of sugar. A patient can be regarded as resistant to insulin only if, after an injection of insulin, the blood sugar is reduced less than is generally the case under comparable conditions. Renal diabetes cannot be regarded as resistant to insulin. Its behavior toward insulin is just like that of the normal organism. The persistence of the glycosuria in spite of the reduction of the blood sugar is caused by the reduced renal threshold. The author further gives his attention to the extra-insular, epinephrinogenic diabetes. This type of diabetes, which is caused by a hyperfunction of the counterregulation, is generally not resistant to insulin. Only a great increase in the action of epinephrine may temporarily impair the function of insulin. Hepatogenic diabetes likewise cannot be regarded as resistant to insulin. Resistance to insulin in case of hyperglycemic diabetes due to insulin deficiency is caused by inactivating substances in the blood, by the influence of fever and especially by the effects of acidosis. From the clinical point of view it is possible to differentiate two types of resistance to insulin, those without and those with acidosis. In many cases an apparent resistance to insulin is simulated by an unsuitable distribution of the doses of insulin. In case of coma with resistance to insulin it is possible to break the resistance by the intravenous administration of alkali. This measure is effective even if the largest doses of insulin have proved ineffective.

Action of Crystalline Insulin on Blood Pressure and Electrocardiogram.—Heinrich and Sussner state that the literature contains contradictory reports about the effects of insulin on blood pressure, respiration and the electrocardiogram. It has been shown that the various brands of insulin available on the market are not of a uniform nature and that some contain substances which act on the circulation. The authors suggest that some of the reported results might be due to these substances. They decided to study the action of crystalline insulin. Their tests were made on rabbits. They were able to show in these animal experiments that, following the injection of crystalline insulin, there is always a decrease in blood pressure, which is not a result of the hypoglycemia but of the crystalline insulin itself. Bradycardia and a lowering of the T wave was likewise observed in many instances. Once an arrhythmia was registered. All these manifestations were chiefly the result of the crystalline insulin. Only the repeatedly observed acceleration in the respiration must be regarded as a manifestation of hypoglycemia. The authors further investigated to what extent the changes that are elicited by crystalline insulin can be influenced by medicaments. They found that when metrazol was administered the decrease in blood pressure, which lasted only seconds, was followed by an increase that persisted for minutes. Electrocardiographic tests frequently revealed that the T wave, which had become lower under the influence of crystalline insulin, showed a tendency to rise again. The effect of metrazol on the frequency varied in that acceleration or retardation occurred. The content of blood sugar was not influenced by metrazol. The authors discuss the mode of action of metrazol in the hypoglycemia that is elicited by crystalline insulin and point out that, since the described circulatory action of metrazol is of only limited duration, repeated injections of metrazol can be recommended for the prolongation of the hypoglycemia during insulin shock therapy. The combined application in one session of insulin shock therapy and metrazol shock therapy does not seem advisable, at least as far as can be estimated from observations on animals. However, no objection can be made regarding the circulation to the alteration between insulin shock and metrazol shock at daily or longer intervals.

Wiener medizinische Wochenschrift, Vienna

88: 113-144 (Jan. 29) 1938. Partial Index

Chronic Polyradiculitis. L. Bieder.—p. 116.
Symptomatology of Narcolepsy and Related Conditions. L. Deutsch.—p. 120.
*Attempt at New Therapy of Narcolepsy. L. Fessler.—p. 125.
Rhythmic Myoclonia of Musculature of Pharynx with Anomalies of Respiration and Heat Regulation. Klara Grünwald.—p. 127.
*Relations Between Mumps and Later Nervous Disturbances. Hermine Lichtenstern.—p. 130.
"Cervical Group" of Facial Neuralgias. J. Wilder.—p. 136.

New Therapy of Narcolepsy.—Fessler points out that for symptomatic narcolepsy that is not caused by tumors, syphilis or trauma there is as yet no satisfactory treatment. Nitschke's observation that hibernation of hedgehogs could be prevented by the administration of irradiated ergosterol induced Fessler to try it for patients with narcolepsy. He reports the histories of two cases in which he resorted to this medication. In the first case no treatment of any kind was given during the first eight days and there was no change in the narcolepsy. Thus the objection is answered that change in surroundings alone will produce a considerable improvement in narcolepsy. After the eighth day the patient was given ten drops twice daily. During the first two days of this medication there was no change, but during the subsequent nine days the patient was entirely free from attacks, although there still were times when he felt tired. On the twelfth, sixteenth and twenty-third days after the onset of the treatment, one attack each occurred. After the patient's return to the home surroundings the attacks of narcolepsy recurred when no irradiated ergosterol was taken, but they became much less frequent when it was taken again. For a more objective estimation of the effect of irradiated ergosterol, complete abstinence from alcohol was enforced for weeks. It was found that this reduced the incidence of the attacks of narcolepsy, but only when irradiated ergosterol was given at the same time did the attacks stop completely. In order to avoid excessive dosage and its possible dangers, the calcium content of the serum was kept under constant supervision: it remained approximately normal. In the second case the medication with viosterol was not quite as effective as in the first. The second patient was much older than the first one and the treatment was begun with smaller doses. When complete abstinence from alcohol was enforced and comparatively large doses of irradiated ergosterol were given, the attacks of narcolepsy ceased.

Mumps and Later Nervous Disturbances.—Lichtenstern reviews the literature on the later sequels of mumps and then reports her observations on 664 women and 520 men who were admitted to a hospital for nervous diseases. Of the women 105 and of the men forty-seven had supposedly had mumps. It was the author's aim to determine whether there are diseases which are especially frequent in patients who have had mumps. She realizes that the number of cases of mumps is too small to allow definite conclusions, but she nevertheless investigated the possibility of a correlation between mumps and later disorders. Summarizing her observations she says that in the patients who had had mumps she noted a high incidence of hepatic disorders, diseases of the gallbladder, infectious diseases, appendicitides, articular disturbances and neurasthenic syndromes. A relative predominance of chronic cerebral or meningeal symptoms, particularly of headache, was not observed. Endocrine disturbances were likewise not especially frequent. In the men who had had mumps, sexual disturbances and arteriosclerosis were even less frequent than could have been expected on the basis of averages. The relatively higher incidence in infectious diseases was to be expected if it is considered that persons who are more susceptible to infections are also more subject to mumps. In view of the presumably different etiology of arthritides, their comparatively high incidence is not readily understandable. Discussing the great frequency of cholecystopathies and of hepatic disorders, the author says that only hypothetical considerations are possible so far. She suggests that the occurrence of a primary impairment of the pancreas during epidemic parotitis might result in a secondary impairment of the liver.

Problemy Tuberkuleza, Moscow

Pp. 1-146 (No. 10) 1937. Partial Index

A Unified Law in Campaign Against Tuberculosis. M. Boldyrev.—p. 3.
Phenomenon of Bordet in Pathogenesis of Tuberculosis. P. O. Drabkina.—p. 7.
Disseminated Pulmonary Tuberculosis of Hematogenous Origin and Course. F. Mandelshtam.—p. 18.
Disseminated Pulmonary Tuberculosis in Children. P. P. Litova.—p. 26.
*Tuberculosis of the Tonsils. S. I. Libin and M. V. Travushkina.—p. 67.
*Erythema Nodosum an Allergic Reaction in Tuberculosis. N. A. Tsukkerman and P. T. Rybak.—p. 75.

Tuberculosis of the Tonsils.—Libin and Travushkina state that, in the belief of most authors, the tonsils of patients with pulmonary tuberculosis become secondarily infected through the sputum. Primary tuberculous infection of the tonsils is believed to occur rarely. The authors found on necropsy of 3,509 cases of pulmonary tuberculosis 605 cases of tuberculosis of the tonsils among 936 cases of tuberculous lesions involving the buccal cavity. The authors made a microscopic study of the tonsils in fifty necropsies in which death had resulted from pulmonary tuberculosis. A clinical diagnosis of tuberculous infection of the tonsils was made in two cases in this group. Anatomic diagnosis was made in seventeen cases. On microscopic observation, a diagnosis of tuberculous infection was made in twenty-seven cases in the absence of any macroscopic lesion. The difficulty in making a clinical diagnosis of tuberculosis of the tonsils is due to the fact that the process develops from the interior of the organ and spreads toward the periphery rather than in the reverse order. This fact likewise suggests that the infection takes place by way of the blood supply rather than by the sputum containing tubercle bacilli. The hematogenous origin of the infection is further supported by the fact that the microscopic evidence of tuberculosis was bilateral in all their cases but one. The authors conclude that tuberculous infection of the tonsils in patients with pulmonary tuberculosis is a frequent occurrence, even though it is not recognized with great frequency clinically or at necropsy. They believe that tonsillar tuberculosis is of considerable clinical importance so far as it contributes to the general intoxication of the organism and gives rise to metastases. The microscopic form is predominantly that of productive inflammation with but few demonstrable tubercle bacilli or with none. The exudative form with ulcerative lesions, considerable necrosis and numerous tubercle bacilli was encountered but rarely. The question of the mode of infection cannot be determined from microscopic studies. The hematogenous route probably plays the most important part in the tuberculous infection of the tonsils.

Erythema Nodosum as Allergic Reaction in Tuberculosis.—According to Tsukkerman and Rybak, a number of observers pointed out that children suffering from erythema nodosum react to tuberculin with great intensity. Thus the sensitivity to tuberculin in such children was in many instances increased to the point of reacting to dilutions of 1:1,000,000, whereas reactions to dilutions of 1:100,000 or 1:1,000 is the rule. The sensitivity to tuberculin is moderate or negative before the appearance of the eruption. With the rise of the temperature and the appearance of the eruption it becomes greatly heightened. The eruption thus coincides with hyperallergy. At the same time pathologic increase of roentgenologic shadows at the root of the lung become demonstrable. The authors emphasize that erythema nodosum is not to be considered a tuberculous lesion. From an anatomic point it is not a tuberculous process. While children with erythema nodosum react to nonspecific bodies as well, such reactivity is transient, whereas the reactivity to tuberculin persists. In fourteen children recently recovered from erythema nodosum, the authors found a positive reaction to the tuberculin. In twelve it was intense, exhibiting vesicles on the surface of the papules in some. A diagnosis of tuberculous infection was made in all of the group. Of these, eight had tuberculous broncho-adenitis, two had pulmonary tuberculosis, two developed pleurisy with effusion, one tuberculous meningitis and one an allergic state. Roentgenologic examination showed tuberculous infection in all. Contact with open cases of pulmonary tuberculosis was found to have existed in seven. The authors conclude that every case of erythema nodosum in a child must be regarded as one in the acute stage of tuberculous allergy and should be observed as such by the tuberculosis dispensary.